EFFECT OF DOMICILIARY DRUG THERAPY ON THE PREVALENCE AND INCIDENCE OF TUBERCULOSIS

The Madanapalle Tuberculosis Research Unit,
Madanapalle.

1977

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EFFECT OF DOMICILIARY DRUG THERAPY ON THE PREVALENCE AND INCIDENCE OF TUBERCULOSIS.

An Investigation under the
Indian Council of Medical Research.

by

The Madanapalle Tuberculosis Research Unit,
Madanapalle.

Report prepared by

Dr. J. Frimodt-Moller, Mr. G. S. Acharyulu,
and Mr. K. Kesava Pillai.

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ENQUIRY INTO THE EFFECT OF DOMICILIARY DRUG THERAPY ON THE PREVALENCE AND INCIDENCE OF TUBERCULOSIS.*)

I. INTRODUCTION

Before the discovery of modern antibiotics effective in tuberculosis the traditional method of combating tuberculosis were considered to be isolation of the infectious cases in hospitals, sanatoria or special colonies (for persons excreting bacilli inspite of long treatment) and the use of BCG vaccination. These methods were used quite extensively before World War II in Western countries but were not applied on any significant scale in the developing countries, including India. While it has been possible in the countries in the West to provide an adequate number of hospital beds to admit the majority of the infectious cases, it was quite impossible to adopt such a procedure in a country of the size of India. Although the number of beds reserved for tuberculous patients has increased in the post-war period it is very small considering the size of the country and the high absolute number of bacillary cases in India. In 1948 BCG vaccination was introduced by the Government of India with the assistance of the World Health Organization. After a preliminary pilot study conducted by the Union Mission Tuberculosis Sanatorium at Madanapalle which showed that BCG vaccination in Indian children did not cause any serious or harmful local reactions (Frimodt-Moller, 1948 and 1949), BCG vaccination was introduced on a country-wide scale in 1949 by the Central Government with the assistance of the International Tuberculosis Campaign, W.H.O. & UNICEF. In the course of a few years, BCG vaccination teams were operating in all the States in India.

At Madanapalle, the initial pilot study of the immediate effect of BCG vaccination led to the setting up of a Field Research Station under the Government of India, Health Ministry, and the W.H.O. Tuberculosis Research Office with a view to study the epidemiology of tuberculosis, particularly trends or changes in the prevalence and incidence of tuberculosis if modern control methods were applied.

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*) Prepared by Dr. J. Frimodt-Moller, Research Director, Mr. G.S. Acharyulu, Senior Statistician and Mr. K. Kesava Pillai, Statistician.

Reports on the results obtained during the first five years were published in 1960 (Frimodt-Moller, 1960) and reports on the protective effect of BCG vaccination in the Madanapalle Study Population were reported between 1960-1973 (Frimodt-Moller, 1960; Frimodt-Moller et al 1964, 1968 and 1973).

Modern anti-tuberculosis drugs were introduced in India in 1946 when Streptomycin became available. Para-aminosalycylic acid (PAS) followed in 1949 and Isoniazid in 1952. It became soon evident that these three drugs represented very potent anti-biotic and chemotherapeutic agents which could produce marked improvement of pulmonary tuberculosis in patients by reducing and eliminating the bacilli from the expectorate. Whereas Streptomycin and PAS were quite expensive and might cause certain complications, Isoniazid proved to be the champion of the three. It was capable of rendering a high percentage of tuberculous patients sputum-negative even when given alone. The break-through in the widespread use of Isoniazid came when the Tuberculosis Chemotherapy Centre, Madras, showed that Isoniazid in combination with PAS was able to render about 90% of bacillary cases of tuberculosis sputum-negative, even if the patients continued to live under normal, simple home conditions (Tuberculosis Chemotherapy Centre, Madras, 1959). The demonstration that chemotherapy under home conditions was as effective as chemotherapy in hospital led very soon to the idea that chemotherapy, particularly with Isoniazid, if used on a mass scale could be a powerful weapon which could render the majority of bacillary cases non-infectious. However, the Madras investigation which had compared home with institutional treatment was conducted under very special conditions for the purpose of ensuring reliable research results. Could these highly encouraging results be reproduced under ordinary normal working conditions? If they could, it might be possible to give Isoniazid, or Isoniazid combined with another drug, to patients in their homes, and in the course of a year to obtain the conversion of the majority of open cases into sputum-negative, non-infectious cases.

There was, therefore, need to try out Home Treatment with simple drug regimens which should be cheap as for cost of drugs and also cheap as for administration and supervision of the treatment. Such an investigation would have to be conducted on line as similar to ordinary conditions as possible and keeping with the existing health facilities. At the same time the investigation should determine not only the results in individual patients, but also the effect on a community basis.

It was then decided by the Government of India as well as the W.H.O. to let the Investigation be carried out by the Madanapalle Field Research Unit, a part of the Union Mission Tuberculosis Sanatorium. A special Project Committee*) was set up by the Indian Council of Medical Research (I.C.M.R.) which should draw up a protocol for the investigation and supervise and advice the Unit during the conduct of the investigation.

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*) Members of the Project Committee of the Tuberculosis Research Project, Madanapalle, February 1959:- Dr. C.G. Pandit, Director, I.C.M.R., Dr. P.V. Benjamin, Adviser-in-Tuberculosis, Directorate General of Health Services, Govt. of India, Dr. E.J.T. McWeeney, Representative of W.H.O., Dr. Halfdan Mahler, W.H.O., . . . Dr. K.S. Sanjivi, Madras, Dr. K.T. Jesudian, Medical Superintendent, U.M.T. Sanatorium, Arogyavaram, Sri K.K. Mathen, Asst. Professor of Statistics, All India Institute of Hygience and Public Health, Calcutta, the Director of Medical Services, Andhra Pradesh and Dr. J. Frimodt-Moller, Director, Tuberculosis Research Project, Madanapalle.

II. PROTOCOL

for the "Enquiry into the effect of domiciliary Drug Therapy on the Prevalence and Incidence of Tuberculosis".

Section I

INTRODUCTION

1. Objective of the Enquiry: To examine (a) the feasibility of a community-wide and systematic administration of modern drugs to tuberculous patients in their homes, (b) its effect on the prevalence of tuberculosis, and (c) the value of prophylactic chemotherapy of cases with radiologically demonstrable lung lesions suggestive of tuberculosis in preventing their development into infectious disease. The drugs will be such that can be taken by mouth, are relatively non-toxic when given over long periods and are acceptable to a large majority of the patients.

The effect of the measures taken will be assessed by:-

(i) setting up two groups of communities, i.e. towns in the 6,000-20,000 range, of which one will be 'treated', the other remain 'untreated'.

(ii) comparing the prevalence in the 'treated' and 'untreated' towns before and after the trial,

(iii) studying the results of treatment of the index cases by regular X-ray and bacteriological examinations in the 'treated' group according to drug regimens used, e.g. PAS + Isoniazid vs. Isoniazid alone.

(iv) studying the prevalence in the sub-groups mentioned under (iii).

(v) studying the drug sensitivity of the strains of tubercle bacilli before, during and after the trial in the 'treated' and 'untreated' towns.

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(iv) studying the prevalence in the sub-groups mentioned under (iii).

(v) studying the drug sensitivity of the strains of tubercle bacilli before, during and after the trial in the 'treated' and 'untreated' towns.

(vi) comparing the attack rate (incidence) during the first half of the study period with that of the second half in the 'treated' group.

(vii) studying the level of tuberculin sensitivity in the youngest children in the elementary schools in the 'treated' and 'untreated' towns before and after the trial.

Section II

PLAN OF OPERATION

2. Material: A number of small towns between 6,000 and 20,000 in population and situated in Chittoor, Cuddapah and Anantapur districts of Andhra Pradesh, and in Kolar District of Mysore State, all within a distance of hundred miles or so of the Madanapalle Tuberculosis Research Centre, will be selected for the trial. The total population will be 120,000-140,000.

3. After the preliminary sample survey, the towns will be ranked according to prevalence of tuberculosis, and after matching, be randomly allocated to three groups: (i) towns 'treated' with PAS-Isoniazid, (ii) towns 'treated' with Isoniazid alone and (iii) 'untreated' towns. In towns (i) and (ii) the X-ray survey will be continued till the whole population is covered.

4. Prevalence Survey I: All the towns selected for the trial will be examined by mass miniature X-ray Survey. As all surveys hitherto carried out by M.M. X-ray examinations in the region show that about 95% of all bacillary tuberculous cases are found among adults and adolescents, while 5% or less are found among children below 15 years who comprise 35-40% of the total population, the X-ray examinations will

include all persons except children below 15 years of age. The initial sample survey will cover a 20-25% random sample of town blocks, the percentage depending upon the size of the town.

5. All persons whose X-ray pictures indicate lesions of the lung parenchyma, the pleurae and the mediastinal lymph nodes will be examined bacteriologically (by microscopy and culture).

6. All strains of tubercle bacilli isolated by culture will be examined for drug sensitivity to Streptomycin, PAS and Isoniazid.

7. The patients who have shown presence of tubercle bacilli by culture or microscopy will in group (i) be given PAS-Isoniazid and in group (ii) Isoniazid only. The treatment will last 12 months.

8. The prophylactic chemotherapy: All persons in the 'treatment' towns who on X-ray show lesions suggestive of tuberculous origin which are not entirely healed up (fibrotic scars, thickened pleura or mere calcifications) and who have not shown presence of tubercle bacilli will be considered eligible for prophylactic drug treatment. They will be allocated at random to one of the following three groups:- (i) to be treated for 12 months, (ii) for 6 months and (iii) to receive no drugs. The drug regimen will be the same as that used for treating the bacillary cases.

9. Follow-up: All case' allocated to the treatment group as well as to the prophylactic chemotherapy group will be re-X-rayed and examined bacteriologically every three months. This will be continued until the final prevalence survey has been completed (Survey III).

10. If any person in the chemoprophylactic therapy trial should develop active tuberculosis, he will be given the therapy considered most appropriate to his case as determined by the type of lesions and the state of drug sensitivity of bacilli.

11. Contacts: Although children below 15 years of age will not be X-rayed, an exception will be made in 'treated' towns with children in households in which bacillary cases have been detected. Such children between 5 and 14 years of age will be (a) X-rayed when the X-ray Unit returns next time to re-photograph the treatment cases, (b) tuberculin tested and (c) the non-reactors to tuberculin be divided at random into one group to be BCG vaccinated and another group to remain unvaccinated. Contacts of 15 years of age or older already photographed will be re-photographed during Survey II.

12. Survey II: A second survey will be done in the 'treatment towns' after 1-1½ years, i.e. during 1961-62. It will be conducted like the first survey and new cases detected will be assigned to the 'treatment' and the 'chemoprophylactic treatment' groups as done under Survey I.

The purpose of this second survey is primarily to find fresh cases which have occurred since Survey I so that they too can be included in the trial; besides, the data obtained affords an opportunity to estimate (i) the incidence of tuberculosis among persons previously showing normal lung pictures, (ii) the prevalence of tuberculosis among persons who have moved into the towns since Survey I and (iii) among children who have reached the age of 15 since Survey I. Further, it should be possible to estimate (iv) the mortality from

tuberculosis and other causes.

13. Survey III: The third and final survey under the present enquiry will take place 1-1½ years after Survey II, i.e. during 1963-64. It will comprise all the towns examined during Survey I, 'treated' as well as 'non-treated'. In the latter group the blocks already examined in Survey I as well as a similar number of new blocks selected at random will be included in the Survey.

Section III

GENERAL CONSIDERATIONS:

14. General principles in the conduct of the Enquiry:

In order to avoid that any bias shall confound the results, the following precautions will be taken: (i) all X-ray films whether obtained at Survey I, II or III shall be read initially by two independent readers without their knowing to which group the persons X-rayed belong, and for the purpose of comparing prevalence between towns by one independent reader from outside Madanapalle, (ii) the bacteriological teams will not be informed about the X-ray findings, (iii) the laboratory staff setting up drug sensitivity tests as well as reading the tests shall not known the identity of the cases at any time, (iv) the doctors, health visitors, technicians and clerk responsible for the supervision of the treatment cases will be kept on rotation between the towns, (v) if the co-operation of a medicinal firm in India can be obtained the drug will be packed and distributed under code names so that none of the staff except the Research Director shall know what type of treatment is given in the sub-groups of 'treatment' towns.

15. Assessment of results: (a) The preliminary sample survey will permit an estimate of the prevalence of tuberculosis this year*) for a group of towns in South India which were not included in the ICMR National Survey of 1955-57 (5,000-10,000 urban populations) besides some in the 10,000 and 20,000 class;

(b) Surveys II and III will provide data for the estimate of the annual incidence, or attack rate, among persons with normal X-ray photographs. An estimate of the incidence of active disease (the break-down rate) among untreated persons with apparantly inactive lesions can be done on basis of observations in sub-group (iii) of the prophylactic chemotherapy trial.

(c) By comparing the prevalence of tuberculosis at Survey III in the 'treated' towns with that found in the 'non-treated' towns, it may be possible to determine if the domiciliary treatment has produced a significant reduction in the prevalence of infectious cases.

(d) Important will be the data obtained at Survey III regarding the type of drug sensitivity of tubercle bacilli in the three groups: (i) towns where patients received PAS-INH, (ii) towns where patients had only INH and (iii) towns where no systematic treatment was introduced.

(e) Finally, there should be sufficient material to know if drugs given prophylactically for 6 or 12 months to X-ray positive cases have been able to prevent the development of active disease.

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*) 1959

Section IV

16. List of towns: within a radius of about 100 miles (160 km.) of Madanapalle (Fig.1):

		Population	Distance
Andhra Pradesh:	Rayachoti	10,700	68 Km.
	Rajampet	9,300	145 "
	Kalahasti	18,000	145 "
	Puttur	8,000	169 "
	Nagari *)	6,600	163 "
	Tiruttani	10,000	182 "
	Kadiri	20,300	80 "
	Punganur	11,300	18 "
	Palmaner	6,900	56 "
Mysore State:	Chintamani	14,400	64 "
	Srinivasapur	6,600	58 "
	Mulbagal	9,000	80 "

*) Later transferred to Madras State (now Tamil Nadu).

17. Time Schedule: With a total of about 16,000 to be photographed, the preliminary sample survey should be completed in about 6 months, and the completion of the survey of the 6 'treatment' towns in another 12 months, the out-put per one mobile X-ray unit being about 25,000 for 12 months.

Preliminary Survey:	June '59 to Jan.	'60
Survey I	: Feb. '60 to Jan.	'61
Survey II	: Feb. '61 to April	'62
Survey III	: May '63 to Dec.	'64

18. X-Ray Code: The code used for the National Tuberculosis Survey of India 1955-57 will be employed. All X-ray abnormal cases will be examined bacteriologically except cases showing conditions which are either clearly extrapulmonary, or, if intra-pulmonary, either clearly non-active (scars, calcifications) or obviously of non-tuberculous origin.

19. Bacteriological examinations will be done in the field and consist of (i) two smears for microscopy, (ii) 2 laryngeal swab cultures, and (iii) a sputum culture from a specimen collected overnight or on the spot when taking the laryngeal swab culture or a pooled specimen if obtained both ways.

20. Drug regimens: PAS: Pas Sodium in granulates, 10 grams per 100 lbs. body weight, Isoniazid: 300 milligrams per 100 lbs. (or 6.5–7 mg. per kilgram). Both drugs to be given daily, PAS divided into 2 doses, INH to be taken in one dose in the morning. All drugs will be issued under code names.

21. Supervision of the treated cases: In each town selected for the 'treatment' group an office shall be opened in a rented house. A home visitor or health nurse will be stationed there, either living in the rented building or elsewhere. A peon will be allotted to each office.

Patients will normally come to the office once a week to get the drugs. The Home Visitor will visit the homes weekly or bi-weekly to check on the amount of drugs in the possession of the patients, collect urine samples for testing excretion of drugs and make general observations.

A medical officer shall be present when the patient is started on drug therapy. He shall personally give the patient all necessary instruction; a written record shall be kept of all instructions given by the doctor or the health/home visitor and any other observations made. The medical officer will return to the office fortnightly the first month, then at least once a month.

The medical officers will be interchanged; and also the home visitors (with two or three monthly intervals).

22. Relationship to private practitioners: If patients already have a doctor or wishes to be supervised by a doctor, a written communication enlisting the cooperation of the practitioners shall be sent to him explaining the situation and the advice given.

23. Normally as little interference as possible will be made in the patient's life and work. The drug therapy will be going on without change unless there is clear clinical and radiological evidence of a deterioration of the condition of the patient. In that case, a change to another drug regimen will be done. Should the case become desperate it may be removed to the R.A.K.T. Hospital*) at Madanapalle.

24. The actual conduct of the three surveys will follow the same pattern as already set up in connection with the National Survey 1955-57. A complete house to house census will be taken in advance of the X-ray examinations. The endeavour will be to cover at least 90% of all X-ray eligible persons.

25. The organisation and follow-up of individual cases at each stage of the investigation will be done in close cooperation with the M.T.R.U. Statisticial Department making use of punch cards to prepare daily, weekly and monthly working sheets to be used by the X-ray and bacteriology departments, the clerical and the medical staff.

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*) The Rajkumari Amrit Kaur Tuberculosis Hospital, Madanapalle, with 60 beds was attached to Madanapalle Tuberculosis Research Unit - both under the direction of the Union Mission Tuberculosis Sanatorium.

III. Comments on the Protocol

Certain alterations and modifications to the Protocol have taken place after the investigation had commenced.

'Prophylactic chemotherapy' (paragraphs 8 and 10): A special study was made of the effects of treatment of cases showing radiological signs of early tuberculosis but with a negative bacteriological result (Frimodt-Moller et al, 1965). The intention described in the Protocol of continuing the study throughout the period of the main investigation was dropped after completing the special study.

'Contacts' (paragraph 11): As the main investigation progressed it was found to be too difficult to keep up a special study of the children who were contacts to families with open bacillary cases and in particular to set up a BCG Control Study. So it was also dropped. However, the members of the family were re-X-rayed at each succeeding survey and if any of the children (below 15 years of age) showed symptomatic evidence of the disease, they were examined when the mobile X-ray units visited their town for routine follow-up examinations.

'Survey III' (paragraph 13): Whereas it was contemplated in the Protocol that the six towns in the "control group" at the time of Survey III should be examined only on a sample basis, a full survey was conducted in each of the six towns similarly to the final surveys in the six "treatment" towns.

'General Principles' (paragraph 14): Under point (i) it was said that the X-ray films obtained at the three surveys should be read not only by the two local readers but also by an independent assessor. This stipulation was dropped as being impracticable and unnecessary as the results of the surveys were based upon the prevalence of bacillary tuberculosis and not on the prevalence of radiologically diagnosed cases.

Only in case of the initial sample survey conducted in all 12 towns before the treatment programme started were the films submitted to an independent assessor so that the prevalence of radiologically positive cases could also be used as an index towards estimating the size of the tuberculosis problem.

The directive given in paragraph 14 (v) that the staff should not know what type of treatment was given in the sub-groups in 'treatment' towns was found to be impracticable and therefore dropped.

'The time schedule' (paragraph 17): The initial time schedule was found to be too tight. The actual time schedule for the three surveys was as follows:-

Survey I: March 1960 to December 1961

Survey II: January 1962 to October 1964

Survey III: September 1965 to January 1969

'X-ray Code' (paragraph 18): Although it was stated in the protocol that certain well-defined cases need not be X-rayed, the general practice was to submit to X-ray examinations all cases whether they were considered to be of tuberculous or non-tuberculous origin.

'Drug regimens' (paragraph 14 (v) and paragraph 20): As quite a high proportion of the bacillary cases offered treatment at home had already been treated elsewhere, it was arranged with a local medicinal firm that they should make large pink tablets containing the prescribed dose of Isoniazid so that patients already treated should not be aware that these tablets contained Isoniazid. PAS was given as Sodium para-amino-salyicylic acid in granulates. Isoniazid and PAS were measured and issued in small paper bags in quantities sufficient for two weeks.

'Supervision of the treated cases' (paragraph 21): The directive of the Protocol that a home visitor or public health nurse should be stationed in each of the treatment towns was also found to be impracticable, partly because of lack of staff and partly because there would not be sufficient work to keep the nurse fully occupied. The 'treatment' towns were visited regularly once a fortnight and each visit allowed the staff

to stay sufficiently long to visit the homes on the same day or the next day but a regular check on the amount of drugs taken or remaining with the patients, and collection of urine samples for testing presence of drugs could not be carried out as a general routine.

'Relationship to private practitioners' (paragraph 22): It was explained to all new cases offered treatment that if they already had a doctor, they could continue to be supervised by him even though they would have the treatment free of charge from our clinics. Also, if patients were receiving Streptomycin and wished to continue to take Streptomycin from their own doctor there would be no objection on part of the Unit. On the other hand, the principle was strictly adhered to that the Unit would not by itself undertake to give injections with Streptomycin.

'Objective of the Enquiry' (paragraph 1): It needs to be stressed again that the objective of the Enquiry was to ascertain whether it would be possible to reduce the prevalence and incidence of tuberculosis significantly by setting up treatment centres having facilities not much different from what could be expected from any Government clinic and using drug regimens which should be available at any Government treatment centre. The initiators of the Investigation had purposely excluded treatment with Streptomycin from the treatment programme of the investigations as they considered this to be too expensive to be introduced on a wide scale if a similar programme should be used on a countrywide scale.

Note on the selection of towns: In selecting the towns the principle was that they should be neither too small nor too large, not too heterogenous with regard to type of population nor should the population be too fluctuating. Therefore, large district headquarter town or towns with railway junctions with staff given to frequent transfers, or towns with temples attracting large crowds of piligrims several times a year, should be excluded. Further, the towns should not be so far away that they could not be managed from Madanapalle as the centre of operation. The towns were therefore chosen within a limit of about 160 km. It was

unavoidable that many roads leading to these towns were of second or third degree so the staff had to travel through rivers, thinly populated areas or jungles. During the monsoon season when the rivers were often impassable detours of many miles had to be done.

IV. BACTERIOLOGICAL METHODS

Isolation of Tubercle Bacilli from Expectorates:

The standard method used in the U.M.T.S. Laboratory for purpose of homogenisation and decontamination when culturing sputa for tubercle bacilli was for many years 6% sulphuric acid (H_2SO_4). Equal amounts of expectorates and H_2SO_4 were mixed and kept in incubator for 20 minutes, then centrifuged, decanted and the sediment neutralised with a drop of sodium hydroxide. The sediment was then inoculated into two tubes of Löwensten-Jensen medium.

As it had been observed for some time that a number of specimens positive by microscopy had failed to grow by culture, it was suspected that the sulphuric acid was too strong and might kill the bacilli. It was then decided in 1964 to change over from 6% sulphuric acid to 4% sodium hydroxide (NaOH); after centrifugation the sediment was now neutralised with a drop of nitric acid.

It was soon found that the change meant a great improvement in the culture technique. The smear positive specimens rarely failed to grow by culture and the number of positive cultures from specimens negative by smear showed a much higher number of positive cultures than before. To get a numerical expression of the advantages obtained by the new methods, a special study was made in 1966.

Over a period of several months all routine specimens obtained in the field were divided into equal aliquots of which one set was treated with sulphuric acid and the other with sodium hydroxide. The culture bottles were given code numbers so that neither the technician nor the bacteriologist who read the culture bottles would know which method had been used. The results obtained are shown in Table I. The sulphuric acid method produced 66 and the sodium hydroxide method 139 positive cultures whereas only 48 of the same specimens were positive by microscopy. Of the 48 specimens, 33 or 69% only were positive by culture when using H_2SO_4 whereas all 48 specimens were positive when NaOH was used. Evidently 15 of the 48 specimens positive by smear and treated with H_2SO_4 had failed to grow. The difference in yield is equally striking when noting that among the specimens negative by microscopy only 33 cultures were obtained when using H_2SO_4 against 91 obtained when NaOH had been used. Of the 91, 33 were positive by both methods and 58 positive by NaOH but negative by H_2SO_4. Table I(b) compares the results by culture with the number of bacilli noted in the specimen which were positive by microscopy. When the smears showed +++ or ++, the number of positive cultures were nearly the same. Of 34 specimens showing 1+ bacilli by microscopy, only 20 gave growth with H_2SO_4 against growth in all 34 cases treated with NaOH. The advantage obtained by switching over to NaOH from H_2SO_4 is even more striking when it is noted that over and above the 49 specimens positive by microscopy, the NaOH method produced 91 positive cultures against only 33 by the H_2SO_4 method.

NOTE: The present investigation began in 1959 and concluded in 1968. The improvement in culture technique took place early in 1964. The Sample Survey and Survey I were done with the old culture technique. The change took place in the midst of Survey II and Survey III was done wholly with the new method. This has an important bearing upon the estimates of the prevalence and incidence of tuberculosis at different points in time during the investigation.

DRUG SENSITIVITY TESTS

The minimal inhibitory concentration (MIC) was defined as the lowest concentration of the drug which inhibited growth of 20 or more colonies.

Definition of drug resistance expressed as MIC of the drugs:

Isoniazid : Culture resistant if MIC is 5 mcg/ml or more.
Doubtfully resistant if MIC is 1 mcg/ml.

Streptomycin : Culture resistant if the resistance ratio (RR) was 32/4 or more;
doubtfully resistant, if RR = 16/4.

PAS : Culture resistant if RR is more than 8/2
doubtfully resistant if RR = 8/2.

A culture of "H37rv" was used as standard strain.

Note: As routine procedure all cultures of tubercle bacilli obtained were tested for susceptibility towards Isoniazid, Streptomycin and PAS. In the present report, however, only the Isoniazid results are included.

Doubtfully resistant strains:

For the purpose of the present analysis all cultures classified as 'doubtfully resistant to Isoniazid' have been counted as 'resistant to Isoniazid'.

The implications of this decision can be gathered from the following observations. (i) Analysing the results of all routine sensitivity tests carried out in the Research Laboratory in the months of March 1965, 1966 and 1967, it was found that of 551 cultures examined 61.3% were INH-sensitive, 31.8% INH-resistant and 6.9% 'doubtfully resistant to INH'. By additing the doubtfully resistant strains to the resistant, the latter was increased from 31.8 to 37.8%, i.e. an increase of 18.9% or - in other words - of strains now classified as INH-resistant 18%, or about one-fifth, would be 'doubtfully resistant to INH' and four-fifths

INH-resistant, (ii) As for the consistency of demonstrating strains 'doubtfully resistant to INH', an analysis of repeat INH sensitivity tests on cultures noted as 'doubtfully resistant to INH' carried out between March 1st 1965 and February 28th 1966 showed that of 107 repeat tests 14 cultures were classified as INH-sensitive, 75 as 'doubtfully resistant to INH' and 18 as 'INH-resistant'. The original classification was therefore confirmed in 70.1% while 16.8% were found to be resistant and only 13.1% of the strains were classified as INH-sensitive.

The merging of strains 'doubtfully resistant to INH' with INH-resistant strains appears justified as the chance of wrongly classifying 'INH-sensitive strains' as INH-resistant may not exceed 2-3 per cent.

V. <u>The Preliminary Sample Survey, 1959</u>.

The main purpose of this survey was to establish a base line indicating the initial size of the tuberculosis problem, absolutely as well as relatively. The Sample Survey was also intended to provide criteria for allocating the towns to the three treatment groups outlined in the protocol, namely, (i) towns in which the only drug issued would be Isoniazid, (ii) towns in which Isoniazid as well as PAS would be given, and (iii) towns where no treatment would be given. On the advice of Dr. K.K. Mathen, Professor of Statistics, and member of the Project Committee it was decided that the sampling fraction should be 20% except for towns with populations of less than 8,000 where it should be 25%.

The method followed in drawing the samples was as follows:-

(1) A team consisting of a doctor and 4-5 clerks visited the towns and made a study of the outlay of the town and noted the number of households in each block, or definable cluster of houses, by preparing sketches of the different parts of the town.

These sketches were then fitted together at headquarters by a draughtsman as pieces in a jig-saw puzzle to form a large map of the town. The map was then reproduced as a blue print measuring about 60 x 80 cms.; in the case of Kalahasti, the largest town, 3 maps had to be made to cover the whole town. Although the maps by no means were made to scale, an idea of the distances were arrived at by letting a jeep run up and down the main street a couple of times to measure the diameter of the town. Thereafter the blocks on the map were encircled with red corresponding to not less than 20 and not more than 40 households per block. In some cases the blocks were so crowded with families that they had to form a special stratum containing over 40 households per block. The blocks were numbered in serial order and samples of either 20 or 25% were drawn by consulting a table of random numbers. Thereafter, a complete census was taken of the persons living in each of the sample blocks selected. When the census was over, the mobile X-ray Unit visited the town, halting in different places according to the convenience of the staff and the local population. The different localities were visited until about 90% of the residents had been X-rayed. The Research Unit had at its disposal two mobile X-ray Units. As there was some difference in the quality of the X-ray films, the two X-ray Units were interchanged so that each town was served equally by the two units.

All persons aged 15 years and more were eligible for X-ray examination. Children below 15 were therefore excluded. The skiagrams were read independently by two doctors who were experienced in X-ray interpretations. All cases showing radiological evidence of pulmonary pathology according to either one or both readers were then visited by a team from the Laboratory. Sputum was collected for microscopy and culture and two laryngeal swab cultures were made on the spot. The sputum and the cultures

were kept in portable refrigerators from the time of collection till they had been brought back to the Laboratory at the U.M.T. Sanatorium. Smears for direct microscopy were prepared and examined either in the field or at headquarters.

The Sample Survey began in Kadiri in May 1959 and was followed by surveys at Rayachoti and Rajampet in Cuddapah districts, Srinivasapur and Mulbagal in Kolar District and from October 1959 by surveys in Tiruttani, Nagari, Puttur and Kalahasti in Chittoor District. Finally, Palmaner and Punganur were examined in December so that the Sample Survey was completed by the end of 1959. The bacteriological examinations continued, however, during the first two months of 1960.

The number of blocks in the two strata is shown in Table II. Stratum I contains 20-40 households and Stratum II contains more than 40 households. In 8 towns the sample fraction was 20% and in 4 towns with populations of 8,000 and less, it was 25%. Table III shows the number of households counted at the time of drawing the maps of the towns. It also shows the resulting sample fraction varying from 17.7 to 21.6 in the group where it was intended to be 20% and from 24.7 to 25.9 in the group of small towns where it was 25%. The last column indicates the number of persons living in the sample blocks as found by the survey teams when they carried out the census of the sample blocks. The population living in all the blocks as estimated from the sample blocks are shown in Table IV(d). The Table gives the official census populations in the 12 towns as found in the Census of India 1951 Report. From the Census of India Reports for 1951 and 1961, the annual growth rate has been estimated and from this again the populations in 1959. Comparing these estimates there is a fairly close agreement in most of the towns except in

Kadiri and Rayachoti where the populations of the Sample Survey were 60.6 and 69.3% only. The discrepancies are due to our teams not covering the whole official municipality area when carrying out the sample survey.

Prevalence of bacillary pulmonary tuberculosis:

Table V summarizes the work done and gives the results for males and females respectively in each of the 12 towns. The coverage obtained at the time of X-ray examination was close to 90% ranging from 89.1 to 94.3% for males and from 86.1 to 93.2% for females. As children below 15 years of age were excluded from the Survey, the eligible persons are those who were 15 years of age or older, and the persons selected for bacteriological examination of the expectorates/are those who had shown signs of pulmonary pathology according to either one or both of the two local readers. Among those selected for bacteriology, the coverage by sputum examinations was on average 87.6% for males and 91.6% for females, ranging from 82.9 to 82.4 for males and from 79.6 to 97.8 for females.

In estimating the bacillary prevalence per 1000 adults, due regard was paid to the fact that the coverage by X-ray or bacteriology was not complete. Assuming that the persons not X-rayed or examined bacteriologically were absent because of circumstances unrelated to tuberculosis the number of bacillary cases which should have been found if all had been examined was calculated for each sex and age group, and the sum of these were divided by the total eligible males or females and multiplied by 1000 giving prevalence rates per 1000 (Table V).

The prevalence varied among males from 2.5 in Chintamani to 25.4 per 1000 in Kalahasti, i.e. a difference of ten times.

The prevalence rates among females were much lower than among the males, 4.8 compared with 13.0 per 1000. In two of the towns no bacillary cases were found, the samples being too small.

Prevalence of radiologically positive cases of tuberculosis:

Although all the X-ray films taken at the Sample Survey had been read by two readers and selection of cases for bacteriological examination had been based upon their readings, it was possible that they could have been biased as they would know from which towns the X-ray pictures came. All the 70 mm X-ray pictures were therefore submitted to an expert, Dr. Wallace M. Fox, the then Director, Tuberculosis Chemotherapy Centre, Madras. The films (about 17,000) were taken to Madras for study by him. The films were not read in serial order but in a random order so that possible changes in his interpretation would be equally distributed over the whole range of films regardless of the towns.

The classification used by the independent assessor was the one adopted by the Survey Teams which conducted the National Tuberculosis Survey of the Indian Council of Medical Research in the years 1955 to 1958. The origin of this classification and the definition of the different categories are described in a previous communication (Frimodt-Moller 1960).

The cases selected for bacteriological examinations by the local readers and the independent assessor were distributed as follows:-

Reader	Number	Cases with TB
Selected by the Independent Assessor alone	357	(Not examined)
By the Independent Assessor as well as local readers	1033	132
By the local readers alone	730	4
Total ..	2120	136

Of the 2120 cases selected, 1763 had been selected by the local readers and 1390 by the independent assessor; common to the independent assessor and the local readers were 1033. In this group 132 cases were found to be bacteriologically positive. Among the 730 selected only by the local readers, 4 showed presence of bacilli. The 357 cases selected by the independent assessor only were not examined bacteriologically as his readings took place after the field work of the Sample Survey had been completed. It is, therefore, not known how many bacillary cases would have been found had they been examined.

Table VI shows the distribution of the cases selected by the independent assessor according to the 5 main categories. The average distribution in per cent was as follows:-

A.	Probably non-tuberculous ..	181	13.1%
B.	Probably tuberculous but inactive ..	79	5.7%
C.	Probably tuberculous and possibly active ..	615	44.4%
D.	Probably tuberculous and probably active ..	406	29.3%
E.	Etiology uncertain ..	105	7.6%
	Total ..	1385	100.1%

Whereas the independent assessor considered 13.1% probably non-tuberculous and 7.6% too uncertain to be classified, 79.4% were thought to be probably of tuberculous origin; 73.7% were considered to be either possibly or probably active tuberculosis. The distribution of the two main groups, C and D, have been merged together for the purpose of working out a suitable index enabling the ranking of the 12 towns according to prevalence of tuberculosis. This is shown in Table VII. The prevalence ranged from 3.9 at Palmaner town to 9.1% at Kalahasti.

Prevalence of tuberculin reactors among school children, aged 5-9:

In order to provide a third index of the prevalence of tuberculosis in the towns, children in the first two grades of all the schools in the 12 towns were given Mantoux tests with 1 T.U. of the PPD tuberculin Rt23 (+Tween 80). Table VIII summarizes the work done and gives the mean percentage of children showing indurations measuring 6 mm or more in cross diameter, on the 2nd, 3rd or the 4th day. Of 4052 children whose tests were read, 630 showed scars resembling scars following a BCG vaccination. They have been excluded.

In most of the towns, reasonably good cooperation was obtained but in some of the towns the school headmasters were non-cooperative as they thought that the parents might object to the tests thinking that they were actually BCG vaccinations. At the time of the survey a newspaper campaign against the introduction of BCG vaccination was taking place.

Frequency distributions of the diameters of indurations to the Mantoux tests are given in Appendix Table I and Graph 1.

Randomisation of the 12 towns into three treatment groups:

The results of the Sample Survey were submitted to Dr. K. K. Mathen of the All India Institute of Public Health and Hygiene, Calcutta. The three indices: (i) the prevalence of bacillary cases per 1000 adults, (ii) radiologically active cases per 100 and (iii) the tuberculin reactors among young school children also in percent are shown in Table IX. The wide range between the lowest and highest prevalences and the close correlation between the three indices are shown in Graph 2. The diagram to the left shows the correlation between the 12 town

prevalences of the bacillary cases and the radiologically active cases and the right side shows the correlation between the bacillary cases and the tuberculin reactors among the small school children. On the basis of these data Dr. Mathen ranked the towns in the following descending order:-

1. Kalahasti
2. Rayachoti
3. Puttur
4. Rajampet

5. Nagari
6. Kadiri
7. Tiruttani
8. Sreenivasapur

9. Chintamani
10. Mulbagal
11. Punganur
12. Palmaner

The 12 towns were then divided into two groups (Table X) of which the 6 (T1 and T2) formed "Treatment towns" and the other 6 the "Control towns". The "Treatment towns" were sub-divided into two groups of which the patients in Kalahasti, Kadiri and Palmaner would receive Isoniazid and PAS and the patients in Rajampet, Tiruttani and Chintamani Isoniazid only. The differences between the mean prevalences of bacillary tuberculosis of the 'T' group and the 'C' group as well as between the 'T1' and the 'T2' groups were statisticially insignificant. The randomisation would appear to have produced three well balanced groups.

VI. DOMICILIARY DRUG THERAPY

When the allocation of the 12 towns to the three experimental groups: (i) treatment with Isoniazid-PAS, (ii) treatment with Isoniazid and (iii) the no treatment - "control" group had been done, the main investigation was taken up. Whereas no further action was taken in the 6 "control" towns, the 6 "treatment" towns were surveyed one by one. Survey I began in March 1960 and

the towns were examined in the same order as during the Sample Survey the previous year. The sample blocks already examined were not re-examined but the cases then detected and any new ones presenting with symptoms were registered as patients due for treatment. The 75-80% blocks not examined previously were now covered by a house to house census followed by X-ray examination of all the persons except children below 15 years of age. The X-ray pictures were studied by two doctors and all persons with signs of pulmonary pathology whether tuberculous or non-tuberculous were referred for bacteriological examination. This was done in the same way as described under the Sample Survey, except that from the beginning of 1964 when the change in the culture technique was introduced the setting up of 2 laryngeal swab cultures was discontinued.

In each of the six towns a house was rented which became the sub-centre or branch office of the Madanapalle Research Unit. It served as office and provided quarters and kitchen facilities for the staff which attended to the fortnightly clinics held on the same premises, and for the X-ray and laboratory staff whenever they visited the towns. The clinics were held on special week-days every fortnight. The team consisted of a nurse or a public health nurse or a social worker, one or two paramedical workers or clerks and a driver. A doctor from the Madanapalle Centre visited the clinics once a month and saw the patients, particularly the new ones, and informed them about the diagnosis based on the X-ray and bacteriological examinations, and explained the need for their treatment for a period of at least one year. History was taken, case sheets entered, body weights recorded and detailed instructions given how the patients should take the drugs at home during the fortnight till the next clinic was held. The

Medical Officer saw not only the new patients but also those who were irregular in attending the clinics or stayed away from the drug issues.

With regard to follow-up examinations by X-ray and bacteriology, in addition to the first X-ray examination done as part of the survey, a second miniature X-ray photograph was taken of all cases referred for bacteriological examinations, so that the diagnosis could be supported by comparing the two skiagrams. No case was considered eligible for treatment unless bacilli had been demonstrated either by microscopy or by culture (or both) but in cases where no bacilli were found a decision was taken whether they should be followed-up or not. The rolls containing the survey X-ray films were not cut but kept in serial order for later reference whenever necessary. All follow-up films including the one taken at the time of the first bacteriological examination were cut and mounted on special cards so that they could be easily handled, examined and filed away in special envelopes which would also hold pictures taken at subsequent follow-up examinations. The case sheets and the mounted small X-ray films in the envelopes were carried in handy trays in the jeep to the sub-centres whenever the doctors visited the clinics.

The treatment consisted of Isoniazid 300 mgms. for a patient weighing 45 kilograms i.e. 6.7 mgms. per Kg. and adjusted for patients weighing more or less. Isoniazid was made up in special fairly large pink tablets so that they looked different from the Isoniazid tablets ordinarily bought in chemists' shops. The PAS was issued as granulate of sodium para-amino-salicylate. This was given in doses of 10 gms. for a patient of 45 Kgs. and adjusted for persons weighing more or less. The PAS issued was the same brand which was ordinarily obtainable at the chemists' shop. The drugs were issued free of charge.

Follow-up Examinations:

Patients under treatment or under observation were re-examined every three months by X-ray and sputum examinations, in the seond year by X-ray twice a year and sputum examinations every quarter and in the third year (and thereafter) by X-ray once a year and sputum examinations twice a year. Should the patients suffer a relapse and treatment be resumed they were re-examined as often as in the first year.

All bacillary strains isolated by culture were tested for sensitivity to Isoniazid, Streptomycin and PAS, and from 1964 tested for Niacin, and when required submitted to other identification tests.

Hospitalisation was not used except in very special cases such as haemoptysis, spontaneous pneumothorax or massive pleural effusions. After the first year of treatment patients with strains of bacilli which had developed drug resistance were offered hospital treatment with second line drugs provided special funds could be found for their purchase. A few cases who failed to respond to second line treatment were referred to the U.M.T. Sanatorium for lung resection.

Material:

The total number of bacillary cases encountered in the 6 towns from the time of the 1959 Sample Survey till Survey III had been completed were 1781 (Table XI). Deducting 176 who were admitted so late that they did not have one year of observation, , 1605 cases were available for analysis; of these, 123 died or moved out of the towns before they were contacted for treatment; 1482 cases were offered treatment, of which 1266 accepted and 216 refused.

Extent of Disease and Cavitation:

All the bacillary cases encountered from 1960 in Survey I till 1968 in Survey III have been classified with regard to extent of disease and presence of cavities as seen on the X-ray picture i.e. the first follow-up picture taken at the time of the initial bacteriological diagnosis. All the entries on the card on which the small 70 mm picture was mounted were covered up so it was not possible to know when and where the X-ray pictures had been taken nor to which treatment group the patients belonged. The lesions were classified according to the system adopted by the British Medical Council and used for the classification of the patients seen at the Tuberculosis Chemotherapy Centre, Madras. The extent of disease was sub-divided into six groups:- Trivial (a very small lesion), Slight (a few infilterations), Limited (lesions smaller than the area of the right upper lobe), Moderate (lesions covering an area larger than corresponding to the right upper lobe but less than the area of one lung), Extensive (lesions involving an area greater than one lung) and Gross (all lung field involved). With regard to cavities they were sub-divided into four groups: nil, slight, moderate and extensive.

A total of 1682 cases were classified and the results are shown in Table XII. The material is divided into cases who were found to be sputum-positive by microscopy (M+) and those who were microscopically negative but positive by culture (C+). Summarising the findings, the cases positive by microscopy showed very small lesions in 7.2%, limited lesions in 17.7, moderate in 39 and extensive and gross lesions in 36.2%. Correspondingly cases which were negative by smear but positive by culture showed the following distribution: 26.6, 28.8, 31.4 and 13.3% respectively. It is clear that the cases positive by microscopy

were generally much more advanced than the cases whose bacilli could be found by culture only.

As for cavities, Table XIII shows that in the group which was positive by microscopy initially, moderate and extensive cavitation totalled 54.2% against only 11.9% in the group which was initially smear negative but positive by culture.

Comparison of 'two-drugs' and 'one-drug' towns with regard to extent of disease and cavities:

In Table XII and XIII, the first three towns listed represent the group in which the patients were given Isoniazid and PAS and the last three, the group where the treatment consisted of Isoniazid only. The means of the percentage distribution of each group as shown in the two tables have been entered in Table XIV. The first part of the table refer to the extent of disease and the second to cavitation; each have been divided into two sub-groups of which the first one represents the cases initially positive by microscopy (M+) and the second the group in which the patients had been sputum negative initially but positive by culture (C+). Whether we consider extent of disease or cavitation, the distributions in the two groups of towns are remarkably similar, the differences being statistically insignificant. However, Group C+ shows slightly more advanced cases in the one-drug group as compared with the two-drugs group although the differences are statistically insignificant.

VII. CO-OPERATION OF THE PATIENTS

As the survey progressed and more and more patients were admitted to the domiciliary treatment and the issue of drugs went on at regular intervals, it became increasingly clear that a major problem was the difficulty in getting the patients to take their treatment regularly and not to discontinue it prematurely. Some patients preferred to take the treatment from private practitioners instead of from the clinics of the Research Unit so that they might avoid publicity or be able to take injections with Streptomycin which did not form part of the treatment offered by the Research Unit.

The difficulty in obtaining full cooperation was apparent already from the very beginning. Excluding patients who died or moved out during the interval between the 'survey' X-ray examination from which a provisional diagnosis was made and until the diagnosis could be confirmed by the demonstration of the tubercle bacilli in the sputum, 84.7% accepted and about 15% of the cases refused treatment (Table XV). Among the cases whose initial sputum examination was positive by microscopy, 90.5% accepted the treatment and 9.5% refused; among those who were negative by microscopy but positive by culture, 79.3% accepted and 20.7% refused. The former group representing the more advanced cases had evidently a greater urge to be treated than those with less advanced disease who were only positive by culture. The degree of cooperation varied from town to town. In Palmaner and Kadiri 95 and 93% respectively accepted the treatment as against 74 and 78% in Tiruttani and Chintamani. These findings represent the average for all patients encountered from 1960 to 1968. A possible change during this period in the attitude of the patients towards acceptance of treatment will be discussed later.

What happened to the patients who did accept our treatment? In order to answer this question statistics have been prepared showing how many of the patients available took treatment month by month until the end of the 12th month. Patients who died or moved out of the towns were deducted from each month's quota leaving a balance of cases who were alive and expected to have treatment; the percentages indicate how many of these did have treatment. In Table XVI the first column headed '0 month' shows the percentage of patients who started treatment (this corresponds to the last column of Table XV). The decrease in percentages of patients under treatment is equal to the rate of defaulters. Details according to males and females and the method of sputum examination by which the bacilli were demonstrated first time are given in Appendix Table II. A summary for 'both sexes' is given in Table XVI, showing the percentage of patients under treatment each quarter. The findings for males and females in each of the six towns are shown in graphs 3 & 4; the former (graph 3) corresponds to the towns in which the treatment consisted of Isoniazid and PAS and the latter (graph 4) to the three towns where only Isoniazid was issued.

It was a common observation that the more advanced cases as represented by the patients whose sputum had been positive by microscopy (M+) co-operated more than the less advanced patients whose sputum had been positive by culture only (C+). The patients who had been positive by microscopy accepted the treatment in 90% and during the next 12 months the drop in attendance amounted to nearly 30% so at the end of the year only 63% took treatment (Table XVI). The cases who had been positive by culture only accepted treatment in 79% and defaulted during the year in 30% leaving 50% under treatment at the 12 months. Considering all

cases regardless of type of initial sputum examination or extent of disease the average performance corresponds to 85% accepting treatment, 30% discontinuing treatment prematurely and 56% who were still under treatment at the end of the year.

A summary of the statistical analysis by linear regression is given in Table XVII. The first column indicates the mean monthly percentage of patients treated during the year; this mean corresponds closely to the position of the curve at six months. The second column indicates the mean of the four regression coefficients obtained by fitting lines to the four series of percentages for each towns as shown in Appendix Table II. The regression coefficients indicate the mean monthly defaulter rate in per cent. The overall per cent of patients under treatment at six months were 70.7% and the mean defaulter rate 2.3% patients per month. Table XVII also shows the result of comparisons between the main effects analysed. The same are illustrated in Graph 5. As for sex, the curves for males and females are practically identical; there is no significant difference between them. As for the initial sputum examinations the difference of 15% between the levels of 78% among those positive by microscopy and of 63% among those positive by culture only is highly significant (Table XVII and Graph 5 (centre)). The curves run parallel indicating the same defaulter rate in the two groups. As for the difference between 'drug regimens' (Graph 5 - lowermost) the INH group showed a much poorer response than the INH-PAS group. Not only was the level significantly lower, namely 65% against 77% (Table XVII), but the defaulter rate was 2.48% per month against 2.12% in the INH-PAS towns, the difference between the two rates being highly significant. In order to determine what could be the reason for this difference in response to the treatments given the following analysis was done.

The total number of cases entering into this Investigation were 1781; of these 176 had less than one year of observation. Of the remaining 1605, 1266 accepted treatment and 339 were not treated. The treated patients can be divided into five groups according to the period when they were admitted. The first group corresponds to the cases found at Survey I (1960-61), the second were patients who presented because of symptoms or were observation cases followed up since Survey I who later developed bacillary tuberculosis, the third were cases found at Survey II (1962-64), the fourth were patients admitted between Survey II and Survey III and the last group, the fifth, were those who were detected at the time of Survey III and who had had at least 12 months of observation. As the number of patients in Palmaner and Tiruttani were too few to allow a detailed break-up the present analysis deals only with the four towns: Kadiri and Kalahasti in the INH-PAS-group and Rajampet and Chintamani in the INH-group (Appendix Table III). The attendance rate was a little better among the patients admitted during the two intervals between Surveys I-II and II-III than among those who were found at the time of the surveys themselves. Whereas the monthly rates for all five groups are given in Appendix Table III, the findings relating to the patients diagnosed at Surveys I, II and III are shown in Graph 6. The levels of cooperation were distinctly higher at Survey I than at the two subsequent surveys. Taking Kadiri as an example for the 3 two-drug towns and Rajampet for the 3 one-drug towns, the graph shows that there was no significant difference between the two towns with regard to the degree of cooperation among the patients found at Survey I. The next group of patients belonging to Survey II showed in both towns a marked fall of the attendance rate, and the patients belonging to Survey III showed another marked fall.

These findings indicate that the initial degree of cooperation was high and the same whether the patients lived in the 'two-drug' or in the 'one-drug' towns. They indicate also clearly that there was a marked reduction in the degree of co-operation during the next 8 years, especially among the patients living in the 'one-drug' towns than among those living in the 'two-drug' towns. These observations suggest that as time passed and the general public had had an opportunity to judge the results of the treatment offered a certain disillusionment or apathy set in leading to a marked increase in the rate of defaulters.

VIII. TREATMENT RESULTS

All patients in the six 'Treatment' Towns diagnosed as having bacillary pulmonary tuberculosis were offered treatment either with Isoniazid and PAS or Isoniazid only. They were followed up every three months by sputum and X-ray examinations whether they had treatment or not. The results are based upon observations at twelve months after starting the treatment. If, however, the patients were absent at the 12 months' examination, the results obtained at the 9 months' or 15 months' examinations were also consulted and included in the assessment of the case as found at the end of one year of observation. If any of the sputum examinations at the 9th, 12th or 15th months of examination showed a positive sputum the result was recorded as "TB+". All cultures obtained were tested for sensitivity towards Isoniazid, Streptomycin and PAS, but the results here presented are limited to Isoniazid-sensitivity tests. Sensitivity tests with PAS were not very consistent or reliable so they have been omitted. Comparison of the sensitivity test results obtained with Streptomycin and Isoniazid showed the Isoniazid-sensitivity to be the dominant factor. It made very little difference in

the results whether the bacilli were sensitive or resistant to Streptomycin. The results here presented refer therefore only to the Isoniazid sensitivity.

The basic data for all the bacillary cases encountered during the Investigation are shown in Appendix Table IV. Each group has been divided according to the initial Isoniazid-sensitivity of the bacilli and sub-divided according to the type of sputum examinations by which the bacilli were demonstrated initially. Cases with negative smears but positive cultures shown under the heading 'Positive by culture only'. The results at the end of one year are further sub-divided into those who had died, moved out, those whose sputum was positive (TB+) and those who were negative (TB-) and, lastly, patients who were alive but for whom bacteriological examinations were not available (NE). The cases sputum-positive at the end of one year have been divided into Isoniazid-sensitive and Isoniazid-resistant cases plus a small group of cases (N) where sensitivity tests were not available.

When working out the results in per cent, the cases who had moved out during the year have been excluded. The percentage of patients who died or survived is therefore based upon the total number minus those who left. In working out the percentage of patients who had obtained negative sputum or continued to have positive sputum, the assumption has been made that those who were absent for the follow-up examinations at the end of one year would have shown the same ratio of positive and negative sputum as those who did get examined. Similarly, in estimating the percentage of cases with Isoniazid-sensitive or Isoniazid-resistant strains, it has been assumed that the cases who did not get drug sensitivity tests done at the end of the year would have shown the same ratio of sensitive and resistant cases as those who did get tested.

The results here presented are therefore reduced to three groups, namely the patients who died, the patients who had positive sputum at the end of the year and those who had negative sputum. In the Tables showing the sensitivity to Isoniazid the sputum positive cases have been divided into two groups: the cases with Isoniazid-sensitive bacilli and those with Isoniazid-resistant bacilli.

The results of treatment are discussed under three headings: First, the results regardless of the initial Isoniazid-sensitivity; second, the results according to the initial type of Isoniazid sensitivity and third, a comparison of the results in the towns where the treatment consisted of Isoniazid and PAS and the three towns where only Isoniazid was issued.

Results - regardless of Isoniazid-sensitivity:

The overall findings are shown in Table XVIII. Although the results for each of the six 'Treatment' Towns are given, the discussion is based upon the means only, each town serving as an experimental unit. Considering section (c) of Table XVIII which covers 'both sexes' and gives the findings irrespective of the initial type of sputum examinations, 9% died, 37% remained sputum-positive and 54% were sputum-negative. Dividing the cases into those whose sputum was initially positive by microscopy and those who were positive by culture only, there is a clear difference: the former obtained negative sputum in 47% and the latter in 62%. Further, in the former group 12% died, 41% had positive sputum while in the latter group 6% died and 32% remained positive. The differences are statistically significant ($P = 0.05–0.02$).

The main reason for dividing the material into two groups according to the initial method of sputum examination by which the bacilli were demonstrated is the fact that few tuberculosis centres in India are equipped for culture work and they must, therefore, rely upon microscopy alone. The percentage of cases who had positive sputum by microscopy to begin with varies between 46 and 58% with an average of 51%. So, without access to culture facilities half the cases would be missed. The tables in the present Report giving the results among cases positive by microscopy initially are, therefore, most in line with the results which can be expected from other tuberculosis centres.

In Table XIX the cases have been divided according to sex. The percentage of females who obtained negative sputum was 57 against 53 among the males. The difference is not significant. In the groups "M+" and "C+", there is an advantage to the females, but the differences are not significant.

Cases with strains initially Isoniazid-sensitive:

The material shown in Table XIX has been further divided according to the initial Isoniazid-sensitivity as shown in Table XX. Cases who either had no cultures done at the initial sputum examination or if cultures were available had no sensitivity tests are omitted but can be found in Appendix Table IV. The percentage of patients with INH-sensitive bacilli who obtained negative sputum is greater than the corresponding results shown in Table XIX. This were to be expected as the cases with Isoniazid-resistant bacilli who have a poorer prognosis have been removed. In the group (M+) who had microscopically positive sputum initially, 50% of the males obtained negative sputum and 58% of the females. In the group (C+) which was positive by culture only, 59% of the males and 73% of the females obtained

negative sputum. Considering all positive cases together the results were 55 and 66% respectively.

Cases with strains initially Isoniazid-resistant:

The percentage of "resistant" cases who obtained sputum conversion (Table XX.B) is only about half of that obtained by the cases who had Isoniazid-sensitive strains, and the percentage of patients who died or remained sputum-positive are about twice as high as obtained by the cases with Isoniazid-sensitive strains. There is no significant difference between males and females.

Although the prognosis of patients with Isoniazid-resistant bacilli is clearly worse than that of cases who started with Isoniazid-sensitive bacilli, the present results are not quite as unfavourable as might have been expected. It may be recalled that the present investigation had a different aim from other investigations studying strictly different drug regimens. The patients living in the six 'treatment' towns were not prevented if they so wished from taking other drugs in addition to the Isoniazid-or Isoniazid and PAS issued by our treatment centres. The patients were at liberty to purchase themselves Streptomycin, PAS or other drugs. This may explain that the results of treatment in patients with Isoniazid-resistant strains are better than expected.

Isoniazid-sensitivity of the bacilli isolated by culture at the end of one year:

When considering 'both sexes' (regardless of initial Isoniazid-sensitivity) it will be seen from Table XXI that the cases remaining positive inspite of treatment are almost equally divided among those with Isoniazid-sensitive and Isoniazid-resistant bacilli, namely 18.4 and 15.4% respectively. This in itself is unusual if the results are compared with what is usually seen among hospitalized patients who are given [illegible]

drugs under supervision. Ordinarily, such cases who continue to have positive sputum will have only Isoniazid-resistant bacilli or the majority of them will have Isoniazid-resistant bacilli. The high percentage of Isoniazid-sensitive strains seen here among the cases positive at 12 months is a direct measure of the irregular and inadequate treatment they had received.

There is a difference in the proportion of Isoniazid-sensitive and Isoniazid-resistant strains among the cases initially positive by microscopy and those initially positive by culture only. The former showed one-third with sensitive and two-thirds with resistant bacilli as against three-fourths sensitive and one-fourth resistant among the latter. The difference is undoubtedly due to the fact that the cases with sputum positive by microscopy were more advanced than the cases who were positive by culture only. The differences are statistically highly significant.

The patients who had Isoniazid-reistant strains to begin with and who continued to be sputum-positive at the end of the year, were still Isoniazid-resistant in 96% while 4% were Isoniazid-sensitive.

Comparison of treatment results in "INH-PAS" and "INH" Towns:

It would already have been noted from the tables reviewed that the results among the patients in three towns listed first i.e. Kadiri, Palmaner and Kalahasti, were better than among the patients in the other three towns: Rajampet, Chintamani and Tiruttani. The former had INH and PAS, the latter only INH. The mean results for the three towns in each group are shown in Table XXII which also gives the differences between the means. Considering first 'both sexes' in the group initially positive by microscopy (M+), negative sputum was obtained in 57% in the

the "INH-PAS" group against 37% only in the group which received only Isoniazid; the difference of 20% is statistically highly significant. In the groups positive by culture only, 68% obtained negative sputum in the INH-PAS group as against 55% in the group who received only Isoniazid; the difference of 13% is also statistically highly significant. Considering males and females separately, both sexes on INH-PAS fared better than those on INH alone; the difference was highly significant among the males but the females showed only significant differences when all the positive cases (M+ & C+) are considered together.

Table XXIII shows the results according to the initial Isoniazid-sensitivity. Considering first the cases with Isoniazid-sensitive bacilli, the percentage who continued to be Isoniazid-sensitive until the end of the year was nearly the same whether they belonged to the microscopically positive group, to the culture-positive group or to 'all positive', the differences being statistically insignificant.

It is noteworthy that the percentages of Isoniazid-resistant bacilli at the end of the year were about twice as high in the "INH" treated group than in the"INH-PAS" group. Considering for e.g. the 'all positive' group (M+ & C+), 10.2% in the INH-PAS group were resistant cases as compared with 20.4% in the INH group, the difference being statistically highly significant. It is evident that the chance of developing resistant bacilli of patients who received two drugs was less than that among patients who received only one drug. Expressed in another way, the chances of developing Isoniazid-resistancewere nearly twice as high in the "INH" towns than in the "INH-PAS" towns.

As for the cases with resistant bacilli initially, the difference between the two-drugs and one-drug groups are not statistically significant although the latter does show a higher

percentage of Isoniazid-resistant bacilli at the end of the year than the former.

Treatment Result - if findings by the culture method were omitted:

As has been pointed out several times, last time at the beginning of the present section, Tuberculosis Centres do not ordinarily have laboratories with culture facilities. In the treatment results presented above, both microscopy and cultures were used to determine whether the cases were sputum positive or sputum negative at the end of the year. What would the results have been if the culture method had not been available for assessing the treatment results?

Of the cases reported positive in Table XVIII, the 40.9% in the group "M+" which showed positive sputum can be divided into two: 27.6% which were positive by microscopy and 13.2% which were positive by culture, i.e. about two-thirds were positive by microscopy and one-third by culture. Of the other group, "C+", the 32.2% sputum positive cases consisted of 13.4% who were positive by microscopy and 18.8% who were positive by culture only. If the cases which were positive by the culture method only are excluded as they would have to be if the culture method had not been available, the trestment results would necessarily appear more favourable. For example, in group M+ the mean percentages for "died", "TB+" and "TB-" were 12.2, 40.9 and 47.0% respectively. Ignoring the cases found positive by culture the results would read 12.2, 27.6 and 60.2% respectively. Similarly, in the group which was positive initially by culture only (C+) the results (as shown in Table XVIII) were 6.2, 32.2 and 61.7% respectively. Without the culture cases the results would be 6.2, 13.4 and 80.5% respectively.

This seemingly paradoxical result is due to the fact that among the cases now shown as negative at year's end, there would be many who would have been positive by culture, had the culture method been available. Such cases would constitute about one-fifth of the microscopically negative cases.

IX. FIVE YEARS' FOLLOW-UP

For the purpose of the present follow-up study all cases in the 6 'Treatment' Towns were amalgamated excluding only those who had less than one year of observation. From the number of cases at risk at the beginning of each observation year, those who moved out of the town have been deducted; those who died have been deducted from the number at risk the following observation year. The cases who survived have been divided into two groups according to the result of the sputum examinations by microscopy and/or culture in the proportion found within each observation year assuming that those who were not examined bacteriologically would have had the same ratio of sputum positives and negatives as those who were examined. Graphs 7-11 show three zones of which the uppermost indicates the percentage of cases who died, the second those who were sputum-negative and the third those who remained sputum-positive. The uppermost curve represents the survivors.

Of 1449 cases (Graph 7 and Table XXIV) who had bacilli in the sputum either by microscopy or by culture and who either accepted the treatment from the clinics of the Research Unit or refused, 60% were alive and 40% had died five years later. At the end of the first year 15% had died, 50% had obtained negative sputum and 36% had still positive sputum. Of those who were alive (59.6%) at five years 18.2% or nearly 1/3rd still had positive sputum. The fact that as much as 60% had either died or continued to excrete bacilli indicates the unsatisfactory results obtained

when viewed with the eyes not only of a clinician but especially of an epidemiologist.

The cases who accepted treatment have been analysed with regard to the initial extent of the disease as seen on the pre-treatment X-ray photograph. As seen from Graph 8 (Table XXV) the rate of survivors decreased as the extent of disease increased so that whereas 80% were alive at 5 years among those who had only very small lesions ('trivial' and 'slight'), only 42% were alive of those who had far advanced disease ('extensive' and 'gross'). The old adage from the years when chemotherapy was not yet available that the prognosis was better the sooner the patients reported for treatment, is still valid.

In Graph 9 (Appendix Table V), the cases treated have been divided according to age groups as well as according to the method of the initial sputum examination. The graphs on the left side correspond to the cases whose sputum was positive by microscopy and those on the right to those who were negative microscopically but positive by culture. As pointed out earlier the former group corresponds to the more advance cases and the latter to the less advanced. It is, therefore, not surprising that the percentages of survivors in the group 'positive by culture only' is higher than among those whose sputum was positive by microscopy. With regard to the influence of age the percentage of patients who had died at 5 years were highest at the age 45-54 and 55+. However, the high rate of deaths may correspond merely to the normal increase with age of the mortality by causes different from tuberculosis.

The cases treated have been divided into those whose bacilli were sensitive to Isoniazid at the start of the treatment and those whose bacilli were resistant. Graph 10 (Table XXVI) shows

at one year a marked difference between the two groups as the Isoniazid-sensitive group turned sputum-negative in 58% as against 27% only among the cases with Isoniazid-resistant bacilli. The differences became less apparent the subsequent years although the rate of survivors continued to be lower among the initially Isoniazid resistant cases than among the cases initially Isoniazid-sensitive. Rather paradoxically, the percentage of cases with positive sputum at the 4th and 5th year of observation were lower among those who were initially Isoniazid-resistant than among those who were Isoniazid-sensitive. This can be explained by the special effort made by the Research Unit to offer treatment with second line drugs in hospital from the second or third year of observation as far as funds raised from charitable sources or from the patients themselves permitted. It was possible to obtain sputum conversion in about 40% of such cases who had persistantly excreted Isoniazid-resistant bacilli.

Lastly, Graph 11 (Table XXVII) presents a five years' follow-up of cases according to whether the sputum was negative or positive at the end of one year. There is a marked difference between the two groups. Whereas the sputum-negative cases showed 82% survivors, of which 66% were still sputum-negative, of the other group which had positive sputum at the end of the first year, only 44% survived and of these again only 24% were sputum-negative. This underlines strikingly the prognostic advantage of obtaining negative sputum during the period of initial treatment.

X. MORTALITY

At the 1959 Sample Survey 20-25% of the populations in the 12 towns were enumerated; the remaining 75-80% of the populations in the 6 towns which were selected as "Treatment Towns" were enumerated during 1960-61, the two stages being combined to form Prevalence Survey I. Surveys II and III in the 6 'Treatment' towns were also preceded by a census of all the individuals residing in the towns. The household was taken as the unit for census enumeration. Apart from the common data such as family name, house address and religion, data regarding name, sex, relationship within the household, residential status and approximate year of birth were obtained, and entered in the census files for each individual enumerated in the census. At the time of Surveys II and III, the relevant files from the previous census were also consulted by the census clerks. If the families had continued to stay in the same house as in the previous census there was no difficulty in obtaining the information about persons present in the previous survey but absent in the present survey. If the families had shifted the places of residence from one house to another within the town either in the same locality or in a different locality, they could still be traced. If they had left the towns no further information could be obtained. Of those who were present in the earlier census but not present in the next census, reasons such as death and emigration were noted down. The emigration rate per year varied between 4 and 6% and was nearly the same for the two sexes. With regard to age, the emigration rates were found to be a little lower in the higher age groups i.e. from 45 years and above. The highest emigration rates were observed among females in the age group 15 to 24 years.

Basic information about deaths due to all causes as well as to tuberculosis are given in Appendix Table VI. The average annual death rates per 1000 due to all causes are given in Table XXVIII. As mentioned in our previous report (JFM 1960), it was not possible to obtain enough data to determine the infantile mortality. Children who were born and died between two censuses were usually not recorded. The estimate of deaths in the age groups 0-14 are therefore minimum rates. The rate of death from all causes show considerable variation ranging from 12.3 in Rajampet to 8.3 in Chintamani, a difference of about 33%.

Deaths from tuberculosis per 100000 are shown in Table XXIX. Excluding deaths among children below 16 years, the overall death rates varied from 26 in Palmaner to 151 in Rajampet, a difference of more than five times. The rates of death among males were particularly high at Kalahasti and Rajampet where deaths among males were estimated to be more than 200 per 100000. The death rates increased especially among males after the age of 45 years but these figures include also some deaths from other causes than tuberculosis. It is worth noting that tuberculosis in these two towns (Table XXX) continued to take a high toll among persons in the most active part of life i.e. at the ages 24 to 44 where 1 in 4 or 1 in 5 of all deaths were caused by tuberculosis and that inspite of the availability of modern anti-tuberculosis drugs.

The average rate of deaths from tuberculosis (Table XXXI) was 0.81 per 1000 for both sexes, 1.15 for males and 0.47 for females; this applies to the age groups from 15 years and upwards. Although it was not possible to determine the exact cause of death among the patients who had had tuberculosis and these rates therefore will include deaths from other causes than tuberculosis,

it can be calculated that if the rates given here for deaths from all causes are applied to the populations of patients with tuberculosis they would at the most have caused an exaggeration of the tuberculosis death rates in the age groups 45–54 and 55+ by about 5%. Table XXXI gives the fiducial limits at the 95% level. It can be seen from this that the mortality from tuberculosis have been estimated within rather wide margins.

XI. "POOL OF INFECTIOUS CASES"

In order to study the effect on the community as a whole two approaches have been made: (i) To compare the prevalence of bacillary cases in the 6 towns at three points in time namely, by Surveys I, II and III which took place at the beginning, the middle and at the end of the investigation, and (ii) to study the prevalence year by year of cases proved to be infectious and to note whether there was any change due to the treatment programme. The second approach will be discussed first.

All patients known to have had bacillary pulmonary tuberculosis or who still had it during any of the calendar years from 1960 to 1968 have been entered in Appendix Table VII as "Cases on the Register". Cases who were removed from the community by death or by emigration were struck off the register the following year. All cases whether treated or not, should have had at least one bacteriological sputum examination each year. Those who were not examined bacteriologically in a year were noted as "Not examined".

The definition of cases entered as 'sputum positive' in a particular year required that they should have been positive either by microscopy or by culture, or both, at least once during that particular year. This stipulation does not exclude that

cases could have been examined many times during a particular year and have shown bacilli more often than once. The definition here given indicates that such a person at least once during the year was known to have excreted bacilli which could have transmitted the disease to his or her contacts.

The sputum positive cases have been divided into three categories designated A, B and C. Category A refers to patients diagnosed as bacillary cases for the first time in the particular calendar year. Category B includes patients diagnosed as bacillary cases during the previous year, and Category C comprises patients who were diagnosed any time earlier than the previous year. As long as a patients once diagnosed as a case of bacillary tuberculosis continued to reside in the town, he or she would continue to appear on the Register. As such, any patient or ex-patient would continue to be carried forward from year to year and would be classified each year as being either "sputum positive", "sputum negative" or "not examined" according to the results of the sputum examinations in that particular year.

In order to simplify the argumentation, bacillary cases in Category A have been called "New" cases and bacillary cases in in Categories B and C have been added together under the designation "Old" cases. Although this group is a mix-up of cases with the illnesses of varying duration the great majority had one thing in common, namely, that if their treatment had been effective they should not have been there but appeared in the group designated "sputum negative".

Results

The diagrams shown in graph 12 illustrates well the composition of the cases on the Register with regard to the sputum results and the different categories since 1960 when Survey I

began till 1968 when Survey III was completed. The uppermost curve indicates the total number of cases (per 1000) on the Register. It starts with the cases diagnosed at the time of Survey I and increases from year to year mainly owing to the accumulation of the patients who turned sputum-negative and were keeping well. The second curve from above indicates the number of patients who were examined within each calendar year. The zone between the two curves indicates the patients who were "Not examined". The following zone corresponds to cases whose sputum was found to be TB-negative; the third curve - No.2 from below - corresponds to the total number of cases who had bacilli in the sputum at least once in a particular calendar year. They are divided into two zones, the upper one representing the "old" and the lower one the "new" cases who were diagnosed for the first time in the particular year, i.e. Category A. The prevalence rates of sputum positive cases among "new" and "old" cases as shown in Graph 12 are entered in Table XXXIV.

Graph 12 shows in a striking manner the variation in prevalence of tuberculosis among the six "Treatment" towns. The highest prevalence was found in Kalahasti, Rajampet and Kadiri and the lowest in Palmaner, Chintamani and Tiruttani. The three towns on the left side of the graph correspond to the group of patients treated with Isoniazid and PAS and the three on the right side to the group who received only Isoniazid; therefore, the former contains two towns with a high and one with a low prevalence while the other group consists of one town with a high and two with a low prevalence.

In all six towns the curves have two or three peaks, particularly the second curve from below showing cases whose sputa were positive each calendar year. The peaks correspond to

the years when the surveys were done. Kadiri for instance, shows three peaks, namely in 1960, 1962 and 1965 corresponding to Surveys I, II and III. Kalahasti was examined first time in 1961, second time in 1964 and lastly in 1968.

The inter-relationship of Categories A, B and C is brought out in Table XXXII. It gives the average number of sputum positive cases per 1000 adults per year. In order to be able to calculate the rates, the populations present in each town each calendar year were estimated by interpolation from the census figures obtained at each survey. The rate per 1000 of all cases on the Register each year is given in Appendix Table VII. Table XXXII shows that in average 43% of the cases sputum positive each year were new cases diagnosed within the particular calendar year while 18% were diagnosed the previous year and 40% even earlier. Assuming that ordinarily all cases who would respond to modern chemotherapy would become sputum negative within six months it follows that no case diagnosed earlier than the previous year should excrete bacilli in the year under review; those who did so would either be cases who continued to harbour bacilli inspite of their treatment or be relapse cases. Of the cases diagnosed during the previous year, those detected as early as on January 1st and re-examined as late as on December 31st of the present year would theoretically have an observation period of two years, while cases diagnosed on December 31st the previous year would have had an observation period of only one day if the check-up examination took place on January 1st in the calendar year under review. Assuming that the intake of new cases was equally distributed during the years and assuming also that no case would be positive after the end of the first six months of treatment, the cases in Category B should not contain more than 25% with bacilli in the sputum while 75%

should be sputum-negative. Adding the 75% of Category B (viz. 13%) to the 40% in Category C, it is estimated that of all the patients having positive sputum more than half (53%) must be attributed to failure of the treatment programme for one reason or another.

The six diagrams in Graph 12 have been combined in Graph 13 to show the means of observations (for both sexes) from all the six towns. The lowermost zone represents Category A or "New" cases, while the zone just above it represents Categories B+C or "Old" cases. Table XXXIII shows the distribution according to males and females. Among males, 60% belong to Categories B and C and among females 52%, the difference being statistically significant ($P < 0.02$).

The sputum-positive cases have also been divided according to the method of demonstrating the bacilli within the calendar years. Graph 14 shows the cases whose sputum was positive by microscopy and those positive by culture only. The curve represent the means of the observations in the 6 towns (see also Table XXXV "Total"). The high peak in 1964 coincides with Survey II and the introduction of the improved culture technique. It is noteworthy that almost half the cases (43%) would have been missed had the culture method not been available. Dividing the two groups into "new" and "old" cases, Graph 15 shows that the cases whose sputum was positive by microscopy initially contained a preponderance of old cases, namely, in average 61% "old" and 39% "new" cases. The cases which were negative by microscopy but positive by culture are seen in the upper half of Graph 15; the two groups were almost equally divided, "New" cases found in 49% and "Old" cases in 51%. It can also be seen from the graph that among the cases positive by microscopy there appears to be from 1960 (or 1961) till 1968 a decrease of "new" cases but an increase of the "old" cases.

Table XXXV shows the general means of bacillary cases (per 1000 adults) in the six towns each year from 1960 and 1968 according to "new" and "old" cases as well as according to the method of sputum examination. Regression analysis showed a significant downward trend (b = -0.17°/oo) among the 'new' cases positive by microscopy and a significant upward trend among the corresponding 'old' cases (b = 0.17 °/oo). The regression coefficient of the two curves relating to the cases positive by culture only were not statistically significant.

It is possible that an artificial element may have contributed to the significant trends noted by the regression analysis. The initial prevalence in 1960 was unusually high owing to the cases detected during Survey I, and the curve for the "old" cases was initially very low due to the treatment programmes beginning in that year so that the accummulation of 'old' cases could only take place during the following year or two. Even though it may not be possible for these reasons to attach much importance to the statistically significant regressions mentioned, the findings are important because they demonstrate that opposing trends can be operating simultaneously within the same community. Reverting to Graph 13, it will be seen that even if the findings in 1960 are disregarded there appears to be a downward trend in the rate of 'new' cases as against an increase of the 'old' cases; therefore, the ratio of 'old' cases to 'new' cases tends to increase during the observation period.

As shown in Table XXXV the rates of "all positives" in the "old" (B+C) group (the zone marked "sputum positives" in Graph 13) increased significantly, the correlation coefficient being 0.34 (P less than 0.05).

Isoniazid Sensitivity

Just as a case with only one positive sputum examination during a particular calendar year was defined as a positive case inspite of perhaps many negative sputum examinations earlier or later during the same year, an Isoniazid-resistant case in the "Pool of infectious cases" indicates that Isoniazid-resistant bacilli were demonstrated at least once during the year. It follows that it could happen that under Category A - the 'new' cases - some patients admitted with Isoniazid-sensitive bacilli could have developed Isoniazid-resistance before the year was out. For this reason, the rates of Isoniazid-resistant cases under Category A do not represent the true incidence of primary INH-resistance among newly admitted cases.

The annual mean rates in each town of Isoniazid-sensitive (S) and Isoniazid-resistant (R) cases in Categories A and B+C according to method of sputum examination are given in Table XXXVI. The means of the 6 towns are shown in the last row of the table and the findings are further analysed in Table XXXVII. Setting the total rates (Table XXXVII) equal to 100% the Isoniazid-resistant cases represented 38% of all the cases. They were mainly found among 'old' cases (Categories B+C), namely in 51.8% while the 'new' cases (Category A) showed only 20.9% resistant cases. Sub-dividing the 'old' cases (Category B+C) into those positive by microscopy and those positive by culture only, the former (M+) contained 61% and the latter (C+) 37% resistant cases. Of the total of 2.45 resistant cases per 1000 (corresponding to the 38.4% mentioned earlier), 0.58 or one-fourth (23.7%) were found among the 'new' cases and 1.87 or three-fourths (76.3%) among the 'old' cases. Among the latter 1.35°/oo, or more than half (61%), were found among the microscopically positive cases brought forward

from the previous year. It seems undeniable that the presence of such a high proportion of Isoniazid-resistant cases among the drug-failure cases presents a formidable problem whether the question is what further treatment to give them or what to do about the high risk in the community of infection with resistant bacilli.

One-drug vs. two-drugs' Towns:

A comparison of the findings in the three towns where the treatment consisted of Isoniazid only and the three towns where it was Isoniazid and PAS are given in Table XXXVIII. The total rates of sputum-positive cases are greater in the INH-PAS towns than in the INH-towns. This is because the INH-PAS group contains two towns with high and one town with low prevalence whereas the INH group contains one town with high and two with low prevalence. Considering the 'new' and the 'old' cases, Table XXXVIII shows that in both, the INH towns showed a higher percentage of INH-resistant cases than the INH-PAS towns. It is particularly striking among the 'old' cases which in the INH-PAS towns consisted of 43% INH-resistant cases against as much as 59% in the INH towns. The differences between the two treatment groups are statistically significant ("New", $P < 0.02$, and "Old", $P < 0.01$). The differences are borne out very clearly in Graph 17.

The conclusion is that treatment with Isoniazid only had produced a significantly higher proportion of Isoniazid-resistant cases, particularly in the group of "Old" cases, than the treatment with INH-PAS.

XII. THREE PREVALENCE SURVEYS

The six 'Treatment' towns were examined three times: Survey I in 1960-61, Survey II in 1962-64 and Survey III in 1965-68. A detailed time-table is given in Appendix Table X. The average interval between the surveys were 29 months from Survey I to Survey II and 50 months from Survey II to Survey III; altogether from Survey I to Survey III, the average interval was 80 months. The time-table does not include the Sample Survey done in 1959 but covers the period spent on examining the remaining 75-80% blocks of the 6 'Treatment' towns not covered in 1959. However, in the Tables showing the results of the three surveys, the results obtained in the sample blocks are included under Survey I. The 6 'Control' Towns were examined during Survey III together with the 6 'Treatment' Towns.

Table XXXIX gives a summary of the work done at the three Surveys. The term 'persons eligible' stands for adults aged 15 years and above. Children below 15 years account for the difference between the total population and the persons eligible. The average attendance rates at the X-ray examinations at the three surveys were 88.3, 80.3 and 82.5% respectively. The corresponding rates for the examination of cases selected for sputum examinations were 84.5, 88.6 and 88.1%. The increase from survey to survey in total population and number of eligible persons reflects the population growth. As for the 'control' towns examined at Survey III, the coverage by X-ray and bacteriological examinations were 85.0 and 93.1% respectively.

Basic Data:

Appendix Table XI presents in detail the findings at the three surveys for each sex and age groups, the number of persons

eligible, the number examined by X-ray, and among these the number of persons who on account of their X-ray findings as determined by two independent readers were selected for bacteriological examinations. Then follows the number whose sputum were examined and, finally, the number who were found to excrete tubercle bacilli as demonstrated either by microscopy (M+) or if the microscopic examinations were negative by culture (C+).

Prevalence Rates:

Appendix Table XII gives the rates of cases with bacillary tuberculosis per 1000 persons X-rayed per sex and age group. Assuming that the reasons for incomplete coverage at the time of the sputum examinations were unconnected with tuberculosis, an adjustment has been made giving an estimate of cases which ould have been detected if all persons selected for sputum examinations had been examined. Similarly, in estimating the prevalence of the bacillary cases for all males and females in each town an adjustment has been made for incomplete coverage at the time of the X-ray examination. These adjustments have been taken into consideration when estimating the variance for the observations at each survey based upon the sex and age group.

As the main purpose of the Investigation was to compare the results obtained in the six towns in which home treatment was offered to the cases of bacillary tuberculosis, with the six comparable towns in which no clinics were set up or any special treatment offered, and since the former group i.e. the 'Treatment' group itself was divided into two groups of three towns each where the treatment consisted of two drugs in one group and of one drug only in the other group, the basic comparisons have been

between the mean prevalence rates obtained from survey to survey in the different groups concerned. By applying this principle the towns have been given equal weightage although they differed in size of populations. Had the analysis been based on simple summation the larger towns or those with high prevalence of tuberculosis would have unduly dominated over the smaller towns or those with low prevalence.

General Observations:

Appendix Table XII gives the prevalence rates of bacillary tuberculosis according to sex and age. The same are shown in Graph 18 which covers Survey I and II, and Graph 19 which shows the findings at Survey III in the 6 'Treatment' and the 6 'Control' towns. In the two set of graphs the towns have been arranged according to the degree of prevalence starting from above with the towns with high prevalence and ending below with those with low prevalence.

There is a marked uniformity in the results obtained from survey to survey. Not only do the towns keep their rank according to prevalence but also the shape of the curves are remarkably consistent from survey to survey.

Two main observations stand out prominently: The great difference in prevalence between males and females and the high rates of tuberculosis among elderly males. Considering the ratio of males to females, the mean percentage distribution for the 12 towns at Survey III was 76.3% males and 23.7% females giving a ratio M/F of 3.2/1. This represents the general picture. There were however exceptions, e.g. in Chintamani, the females were at Survey I in preponderance, namely 57% as against 43% males; at Survey II the opposite was observed, namely 58% males and 42% females, and at Survey III the findings were 71% males

and 29% females, which is more in keeping with the general observations. However, in Nagari at Survey III, the prevalence rates were 18.4 in males and 2.3 per 1000 in females i.e. 89% males for 11% females, or a ratio of 8/1. As for exceptionally high rates of prevalence it will be noted that in Kalahasti at Survey I, males in the age group 55+ showed a prevalence of over 40 per 1000, or 1 person in 25. Similar rates were found in Rajampet at Survey II and in Puttur at Survey III in the age group "45-54". However, the number of persons in the community reaching the age of 50 to 60 may not be high, so an estimate has been made of the distribution of males and female cases in the community taking the average of the 12 towns examined at Survey III, as shown in Table XL-A.

Table XL-A

Mean Distribution in per cent of bacillary cases in the 12 Towns at Survey III according to Sex and Age.

Age (Years)	Males %	Females %	Ratio M:F
15-	7.6	4.8	1.5 : 1
25-	16.5	5.5	3.0 : 1
35-	21.4	5.8	3.7 : 1
45-	15.9	2.9	5.5 : 1
55+	16.8	3.4	4.9 : 1
Total	77.6	22.4	3.5 : 1

Of every 100 bacillary cases, 77.6 were males and 22.4 females, giving a ratio M/F of 3.5/1. Half of the bacillary cases (54%) were found among males in the age group from 35 and upwards. Even one-third (33%) were found among males in the age group 45 and above. The ratio M/F was 1.5/1 in the age group 15-24, thereafter increasing steadily through 3:1 to 5.5:1 in the age group 45-54.

To sum up: The main sources of infection in the community is dominated by the male patients and among these again by males aged 35 and above.

Mean changes in prevalence between surveys in the 6 'Treatement' towns:

The total prevalence rates for males and females at Surveys I, II & III are shown in Appendix Table XI have been summarized in Table XL. As an example, in Kadiri the prevalence rates for males at the three surveys were 16.9, 10.2 and 15.5 per 1000 males respectively; for females 5.9, 5.1 and 6.1 per 1000 females respectively. These findings have been carried over to Table XLI with the difference that whereas the prevalence rates were hitherto expressed as cases per 1000 adult males or females, they have been recalculated and are now expressed as cases per 1000 adult males and females; therefore, in Kadiri the rates for males at the three surveys are now presented as 8.60, 5.22 and 7.96 respectively; for females: 2.89, 2.47 and 2.95. The rates for "both sexes" are found by addition, namely: 11.49, 7.69 and 10.91 respectively. It may be noted that the rates are about half the former.

The comparisons between the Surveys are based upon the means of the observations in the six towns. For instance, in Survey I (Table XLI) the means for males positive by microscopy was 4.93 while at Survey II, it was 3.77 and again at Survey III 3.67. The difference between the results of the first and the second, and the first and the third survey are shown in Table XLII which also gives the P values of the differences. In the present example the difference between Survey I and Survey II of males with sputum positive by microscopy was 1.16. It was statistically insignificant as the P value was only 0.10 against

this the difference between Survey I and Survey III viz. 1.26 had a P value of 0.05, indicating a significant decrease from Survey I to Survey III.

The main results of the three prevalence surveys are shown in Table XLII. Considering first the cases whose sputum examinations were positive by microscopy, there is a decrease in prevalence from Survey I to Survey II and especially from Survey I to Survey III. This applies to males as well as females and also to 'both sexes'. Considering the latter - 'both sexes' - there was a significant decrease among the cases whose sputum was positive by microscopy (M+), from 6.84 at Survey I to 5.02 at Survey II and to 4.79 at Survey III. Turning to the cases whose sputum was positive by culture only (C+) there was for males as well as for females an increase in prevalence from Survey I to Survey II and from Survey I to Survey III. Considering 'both sexes', it rose from 2.61 at Survey I to 4.92 per 1000 at Survey III. This increase of 2.31°/oo was almost significant at the 5% level, the P value being 0.06. As the rates among the cases positive by microscopy showed a decrease and the cases positive by culture only an increase, it is not surprising that when added together they offset each other so the total results show no important changes from survey to survey.

The decrease in prevalence from Survey I to Surveys II or III of the cases positive by microscopy is considered to be a real decrease which is not explainable merely by changes in the technique. On the other hand, the increase in the prevalence among the cases whose sputum examinations were negative by microscopy but positive by culture is considered to be due to the improvement in the bacteriological technique which took place in 1964 when the homogenizing agent used at the time of setting up primary cultures was changed from 6% sulphuric acid to 4% sodium hydroxide.

Comparison between mean prevalence rates in the three "INH-PAS" towns and the three "INH" towns:

The results are given in Table XLIII. Part A of the Table refers to the 3 towns where the treatment consisted of Isoniazid and PAS, namely Kadiri, Palmaner and Kalahasti, and Part B to the towns where the treatment consisted of Isoniazid only, namely Rajampet, Chintamani and Tiruttani. In the "INH-PAS" group, the cases with sputum positive by microscopy show among the males a statistically significant decrease from Survey I to Survey II and among females from Survey I to Survey III. The cases which were positive by culture only, showed an increase from Survey I to Survey II or Survey III but the difference among males or females do not reach significant levels. However, when both sexes are taken together, the cases microscopically positive showed a highly significant decrease from Survey I to Survey II ($P < 0.01$) and an almost significant decrease between Survey I and Survey III ($P = 0.09$). With regard to the cases positive by culture only, there was an increase from 2.75 at Survey I to 4.62 at Survey III which is almost significant ($P = 0.06$). Turning to the INH. towns, the trend observed among the Two-drugs towns were also noted among them but none of the changes reached statistical significance levels.

The changes from Survey to Survey observed in the "INH-PAS" towns have been compared with the corresponding changes observed in the "INH" towns but in none were the differences statistically significant.

Isoniazid Sensitivity (Tables XLIV-XLVI and Appendix Table XIII and XIV):

All cultures isolated were as a matter of routine examined for drug sensitivity towards Isoniazid, Streptomycin and PAS. In this report only the results of Isoniazid sensitivity tests are presented. The distribution of Isoniazid-sensitive and

resistant strains in the 12 towns according to survey, sex and method of demonstrating the bacilli is shown in Appendix Table XIII. In a few cases cultures were obtained but drug sensitivity tests were missing or the tests not done. Assuming that these cases would have shown the same ratio of sensitive to resistant cases as found among those for which the results are available, the prevalence rates have been worked out and are shown in Table XLIV. The mean of the prevalences of the six towns according to sex and method of demonstrating the bacilli are also found in Table XLIV and summarized in Table XLV which also gives the changes between Surveys.

Part A of Table XLV deals with cases with Isoniazid-sensitive strains. In the males whose sputa were positive by microscopy there were significant decreases from 4.21 at Survey I to 2.20 per 1000 at Survey II and 2.52 at Survey III. The cases where sputum was positive by culture only, the increase in the prevalence rates from Survey I to Survey II or Survey III previously seen was observed again but the differences were not statistically significant. The same was also seen among the females but here too the differences were not significant. However, considering 'both sexes', the cases with sputum positive by microscopy showed highly significant decreases from Survey I to Survey II and Survey III.

Part B of Table XLV deals with cases with Isoniazid-resistant strains. Whereas the previous comparisons among cases whose sputa were positive by microscopy showed a decrease in prevalence from Survey I to Survey II and Survey III, the present comparisons show among males an increase from Survey I to Survey II and also in most cases, from Survey I to Survey III. However, in none were the changes statistically significant. With

regard to the cases positive only by culture, there was an increase from Survey I to the other surveys, and in case of females there was a significant increase from 0.06 at Survey I to 0.47 per 1000 at Survey II. Considering the positive cases irrespective of method of diagnosis, there were statistically significant increases from Survey I to Survey II, in females from 0.67 to 1.14 and in 'both sexes' from 1.58 to 3.33 per 1000.

The Treatment Programme and the Changes in Prevalence:

Comparing the results of the three prevalence surveys conducted in the 6 'Treatment' towns, it was found that even though the total prevalence of bacillary tuberculosis showed no essential change from Survey to Survey, the study of special factors such as the method of demonstrating tubercle bacilli in the sputum either by microscopy or by culture, or the division of the material into Isoniazid-sensitive and Isoniazid-resistant cases, did reveal further changes in the prevalence of the more advanced type of cases (M+) as compared with the less advanced (C+), and Isoniazid-sensitive cases as compared with Isoniazid-resistant cases. The question arises to which extent could the active treatment programme in the 6 'Treament' towns started at the time of Survey I have been responsible for the changes and how much could be due to other causes? In order better to understand the currents ar cross currents which could have been set in motion by the active treatment programme the significance of the observations described in the preceding paragraphs have been summarised in Table XLVI. This table summarizes in a more lucid way the main changes observed. Equalling the observations at Survey I with 100% the corresponding prevalences at Survey II and Survey III are shown as percentages of the rates of Survey I. The table allows the study of three factors:

(i) Considering the possible role of males versus females, Table XLVI shows that whether the changes from Survey I to Survey II or from I to III lead to an increase or a decrease the changes are nearly the same for males or females. It is, therefore, justified to confine the following considerations to 'both sexes' only. (ii) The material in Table XLVI has been sub-divided into three groups, namely according to the method of sputum examination: (a) Cases whose sputum was positive by microscopy (M+), (b) cases negative by microscopy but positive by culture (C+) and (c) all positive cases regardless of method of diagnosis. (iii) Lastly, the material has been divided into three groups according to drug sensitivity, viz., (a) ignoring the Isoniazid sensitivity of the bacilli, (b) cases with Isoniazid-sensitive bacilli and (c) cases with Isoniazid-resistant bacilli.

Table XLVI A - both sexes - deals first with the group of cases positive by microscopy (M+). The prevalences at Survey II and Survey III were only 73 and 70% of that found at Survey I. This decrease which is statistically significant, is not likely to be due to technical reasons but may be due to the effect of the active treatment programme. With regard to the group (2) which deals with the cases which were positive by culture only (C+) there is at Survey II an increase by 59% and at Survey III by 89% over the prevalence at Survey I. This increase is undoubtedly due to the improvement in culture technique which took place mid-way during Survey II so that of the 6 towns surveyed only the last two or three benefited from the improvedtechnique. As it can be assumed that the treatment programme must also have affected this group it seems reasonable to assume that without the improvement in culture technique the rates at Survey II and Survey III would have been lower. Subgroup (3) is the sum of (1) & (2). It is clearly seen that the decrease in per cent observed in group (1) is

offset by the increase in group (2) so that the percentages observed at Surveys II and III do not differ substantially from that of Survey I. If drug sensitivity tests had not been carried out, these results would have been regarded as the final in the investigation and the impact of the treatment programme would at best have been estimated as a 30% decrease from Survey I to Survey III in group (M+). However, owing to the drug sensitivity studies the results are different.

Group B which deals with cases with INH-sensitive-strains the cases microscopically positive (M+) shows a much lower prevalence at Survey II and Survey III than was seen above under Group A. The group 'both sexes' shows a drop of 50% at Survey II and 40% at Survey III since Survey I. The corresponding decreases in Group A above were only 27 and 30%. As for 'males' in the 'M+' group the percentage of INH-sensitive cases at Survey II was 52% but 76% in A(1) and with regard to 'females' with INH-sensitive strains showed only 45% as against 65% in group A(1). Turning to the cases in the 'C+' group, there is an increase of 31% from Survey I to Survey II and of 69% from Survey I to Survey III; it compares with 59 and 89% increases respectively in group A above. In case of group B (3) "all positives", the rates for 'both sexes' at Survey II was 74% and at Survey III 92% of the rates at Survey I.

It is very clear that the changes from Survey I to Survey II and from Survey I to Survey III are quite different when dealing with cases having Isoniazid-sensitive strains as when no attention is paid to the Isoniazid sensitivity. The reason for the lower prevalences among INH-sensitive cases in section B than in section A of Table XLVI is clearly the omission of the Isoniazid-resistant cases from the total positives. Turning now

to Group C - the cases with INH-resistant strains - there is in group M+ ('both sexes') an increase of 69% at Survey II since Survey I. In group C+ the males show at Survey II a three times' increase of INH-resistant cases and the females an increase of nearly 8 times, while 'both sexes' show a four times' increase. Although it was stated earlier that the increases of 59 and 89% from Survey I to Surveys II & III observed in A(2) was due to the improved culture technique it can now be seen that this cannot be the only reason; part of the increase was due to the inclusion of Isoniazid-resistant cases which had emerged between Survey I and Surveys II & III.

By the same argument it can be reasoned that had it not been for the development of INH-resistant cases, the results of 73% and 70% at Survey II and Survey III observed in A(1) would have been considerably lower.

The Six 'Control' Towns:

In pursuance of the original 'Design of Experiment', 6 of the 12 towns examined by Sample Survey 1959 were set aside as 'Control' towns to the 6 'Treatment' towns. When Survey III was carried out in 1965, the 'Control' towns were included in the Survey. So altogether 12 towns were examined between 1965 and 1968. In the Tables giving the results of Survey III the findings in the 6 'Control' towns have also been incorporated. In Table XLI the prevalence rates in each of the 'Control' towns have been given with regard to sex and method of bacteriological examination. The mean prevalences in the 'Treatment' towns and the 'Control' towns have been shown in juxtaposition in Table XLVII. It includes also the differences between the means of the two groups and their standard errors. The results are remarkably alike and none of the differences are statistically significant.

With regard to Isoniazid-sesntivie and Isoniazid-resistant strains, Table XLIV lists the rates for males and females according to the method of sputum examinations. It includes also the findings at Survey III in the 6 'Control' towns. The mean observations in the two groups of towns have been carried over to Table XLVIII which compares the results in the two groups under the headings 'Isoniazid-sensitive strains' and 'Isoniazid-resistant strains'. The results are very similar, and none of the differences between the means in the two groups are big enough to reach levels of statistical significance.

The conclusion is, therefore, that the prevalence of tuberculosis observed in the six 'Treatment' towns at the time of Survey III is very similar to that of the 6 'Control' towns. The fairness of the original allocation of the 12 towns in 1960 into two comparable groups based upon the 1959 Sample Survey has been amply verified by the results obtained 5 to 8 years later by the full survey now covering the whole adult populations. The similarity between the two groups is so great that it has not been possible by a detailed analysis to find a single point which could convincingly point to an effect of the active treatment programme carried out in the one group but not in the other.

Changes in prevalence between the 1959 Sample Survey and Survey III in 1965-68:

The six towns which became 'Control' towns were examined together with the six 'Treatment' towns in 1959. This was done preliminary to the allocation of the 12 towns to the 2 groups. It is, therefore, possible to compare the 1959 prevalence results based upon 20-25% samples of the town populations with the results obtained at the full survey carried out at the time of Survey III. The changes in the prevalence from 1959 to 1965-68 in

each of the 12 towns as observed in 'Both sexes' are given in Appendix Table XV. Here too the material has been subdivided according to the method of sputum examinations. The weighted mean change observed in the six 'Treatment' towns in the group of cases positive by microscopy was 1.118 per 1000 (males and females). The corresponding mean change for the six 'Control' towns was 1.375. The difference between these two was -0.257 with a variance of the difference of 9.454. The difference is insignificant. The same applies to the difference between the weighted mean changes observed in the groups comprising the cases which were positive by culture only; it also applies to the difference between the 'Treatment' and 'Control' towns when all the positive cases were considered together ($P > 0.20$).

Comparison of the mean prevalence of the 12 towns at the Sample Survey in 1959 with the mean prevalence obtained at Survey III 1965-68:

The result of this analysis is presented in two ways. Appendix Table XVI gives the mean prevalences at the two surveys for males and females respectively as well as for both sexes according to the method of sputum examinations. Besides this, the results are presented in graphical form as a series of correlation diagrams. In Graph 20 the two uppermost diagrams indicate the cases whose sputum was positive by microscopy, the middle the cases positive by culture only and the lowermost all the cases whether positive by microscopy or by culture. The three diagrams to the left represent the males and the other three the females. The diagrams bear out strikingly the modest role played by the females as against the almost domineering role of the males. The distribution of town prevalence rates among the females show no correlation between the two survey results in any of the three diagrams. Turning to the males in the topmost diagram (cases

positive by microscopy) 7 of the 12 town prevalences are situated in the right triangle below the diagonal; the diagonal itself indicates towns having the same prevalence at both surveys. Appendix Table XVI shows that the decrease among males in mean prevalence from the first to the last Survey was not significant ($P = \geq 0.2$). The middle diagram which shows the town prevalences based upon the males cases negative by microscopy but positive by culture, 9 points are found in the left upper triangle, namely 3 'Treatment' towns and all 6 'Control' towns. It indicates that the prevalence had increased between the Surveys, and this change (Appendix Table XVI) was highly significant ($P = 0.01$). The distribution of the town prevalences in the lowermost diagram points to a strong positive correlation ($r = 0.84$); the position of 8 towns to the left of the diagonal suggests a modest increase in mean prevalence but this was not statistically significant.

The three diagrams depicted in Graph 21 illustrates the positions when the data for males and females were amalgamated i.e. 'both sexes'. In the group positive by microscopy, 8 points, 4 'treatment' and 4 'control' towns, are found below the diagonal indicating a decrease in the Mean Prevalence; as shown in Appendix Table XVI this decrease of $1.24^{0}/oo$ was almost significant ($P = 0.07$). The middle diagram shows the prevalences in the group positive by culture only. Here 10 points, 4 'treatment' and all 6 'control' towns, are lying above the diagonal. This corresponds to an increase of 1.73 in mean prevalence which is statistically significant ($P = 0.04$). The lowermost diagram relates to all cases regardless of method of sputum examinations. The 12 points are very close to the diagonal thereby indicating that the mean prevalence showed a lsight increase but this was statistically insignificant.

It is interesting that there is such a marked agreement between the findings at the Sample Survey in 1959 and Survey III done in 1965-68 ($r=0.855$; $p = 0.001$). It underlines the value of a sample survey in ascertaining the level of tuberculosis prevalences in selected communities. As the 1959 Sample Survey of the 12 towns was carried out in the course of six months only by means of two mobile X-ray units, each with its own trained staff, such sample surveys provide a valuable tool in assessing the size of the tuberculosis problem and in indicating which sectors of the populations present the greatest risk of tuberculosis. This type of information will be helpful either in setting up treatment facilities or in identifying areas which offer the greatest risk of exposure to infection. It is also worth noting that the observations made at the Sample Survey with regard to the ranking of the 12 towns were still valid 6-9 years later.

XIII. <u>The prevalence of bacillary tuberculosis estimated by means of Surveys I, II & III compared with the estimate of sputum positive cases according to the Register ('Pool of infectious cases'):</u>

A comparison has been made between the mean prevalence of bacillary tuberculosis as found by the three surveys carried out in the 6 treatment towns between 1960 and 1968 and the annual 'period prevalences' described in the section on 'pool of infectious cases'. With regard to the three surveys, the mean prevalence per town was found by fitting a regression line to three survey prevalences and determining the mean value at the midpoint in time, i.e. between 1960-1968, and similarly finding the mean rate of proved bacillary cases per calendar year on the Register or the 'pool of infectious cases' at same point in time. The results are entered in Table XLIX. The comparisons have been done with regard to cases whose sputum was positive by microscopy as well as with those whose sputum was positive by culture only, and also with regard to 'all positive' cases.

There is a remarkably high correlation between the two types of independent estimates. The correlation coefficients in the 3 sets of comparisons were 0.97, 0.91 and 0.95 respectively, - all statistically highly significant.

Although the two methods of determining the prevalences - the survey method and the follow-up method of known cases - differ much from each other with regard to basic principles and the time factor, yet the comparisons give a fairly good idea of the extent to which the Centre (the Research Unit) had knowledge of the bacillary cases existing in the community. From the ratios (S/P) of survey prevalences to 'pool prevalences' in Table XLIX it is seen that the survey prevalences were in average about 50% higher than the prevalences estimated on basis of the annual Registers, or in other words: the latter includes only about 2/3 of the cases detected by the X-ray surveys; so for every one known case there would be another unknown case at large in the community; this applie equally to cases with sputum microscopically positive and cases positive by culture only.

It is evident that the limited or partial coverage of the active case finding and treatment programme revealed by this analysis reduces its impact on the prevalence of tuberculosis in the community

XIV. TUBERCULIN SAMPLE SURVEY 1966-69.

In 1964 a special Investigation was undertaken by the Madanapalle Tuberculosis Research Unit to study the role of mycobacteria of different types in producing skin sensitivity and disease in man.*) As part of this Investigation a Tuberculin Sample Survey was carried out in the 12 towns which formed the basis for the present Investigation. The block size was fixed at 50 households and as the average size of an Indian family is 5.0-5.5, there were about 250 persons per block.

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*) The Study was supported by a grant from the US PL 480 Funds and carried out in cooperation with Tuberculosis Research Program, National Communicable Diseases Centre, Washington Office, US Public Health Service.

Excluding persons who had died, moved out, were out of station or disabled, and excluding children below the age of two years, the number of persons to be tested (Table L) varied from 1500 to 1800 (in Kalahasti 2400**)). The coverage ranged from 52 to 91% with a mean of 72%. The tests were carried out by a trained health visitor who gave the injections as well as read the tests. Injections were given on the first three days of the week and the readings done the last three. The reactions were therefore normally read at 72 and sometimes at 96 hours. The tests were given in the homes. It took about six weeks to complete the testing in a town.

The Mantoux Tests were carried out with two PPD antigens namely Standard Tuberculin or PPD-S and PPD-G, an antigen derived from the scotochromogenic strain "Gause". The PPD antigens were prepared and delivered in readymade solutions at the Tuberculosis Research Laboratory, Chamblee, Georgia, by the Tuberculosis Research Program, Communicable Diseases Centre, Washington. They were kept in a refrigerator until used. The ampoules were issued to the health visitor under code numbers so that she would not know what product she was testing. Decoding at headquarters was done after the completion of each town. Doses of PPD-S corresponded to 5 Tuberculin Units (without addition of Tween 80). The dose of PPD-G was adjusted so that the nitrogen content of the two products was the same. The two tests were given in random order on the volar aspect of either forearm according to plans prepared in the M.T.R.U. Statistical Department. The size of the reactions to the Mantoux tests was indicated by measuring the cross diameter

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**) In Kalahasti the sample included 15 blocks.

of the indurations in mm. After reading the tests the shoulders of each person were examined for presence of BCG vaccination scars.

For the purpose of the present report the sample populations have been analysed according to age groups but not separately for males and females. Only the results of tests done with PPD-S are given here.

The number of persons living in the sample blocks (excluding children below two years) is given in Table L together with the number available for testing, the number tested and the number whose reactions were read. Table LI shows the total number tested and read in all the sample blocks of each town and the percentage of persons whose indurations measured 8 mm or more; they are divided according to age groups. Graph 22 shows the frequency distribution of the percentage of reactors according to size of the induration among 2371 children in the age group 5-9 years from the sample blocks in the 12 towns when tested in 1966-69. Indurations of 8 mm and more were adopted as criterion for reactors.

Results:

Graph 23 shows the mean percentage of reactors according to age in the 6 'Treatment' towns and the 6 'Control' towns at the 1966-69 Sample Survey.

Although the prevalence of reactors to PPD-S tuberculin in the 'Treatment' and 'Control' towns are very similar (Ref. Graph 23 and Table LII), the relative differences are most noticeable in the younger age groups. At the age of 2-4 years the percentage of reactors was 9.6 in the 'Treatment' towns and 4.5 in the 'Control' towns i.e. nearly twice as high in the

'Treatment' towns as in the 'Control' towns, and at 5-9 years it was 18.2% in the 'Treatment' towns and 13.9% in the 'Control' towns; the differences are statistically significant.

The question arises whether the difference in percentage of reactors observed among the small children reflects a similar difference which might have existed before the present Investigation began or whether it could be ascribed to the effect of the domiciliary treatment programme in 6 of the 12 towns. A comparison has, therefore, been made between the results of the 1959 Tuberculin Survey which preceded the present Investigation and the Sample Survey of 1966-69. Table LIII summarises the findings which are also seen in the corresponding correlation diagram in Graph 24. As the graph shows there is a clear correlation between the prevalence of reactors obtained at the two sample surveys; the correlation coefficient of 0.651 is statistically significant (P: 0.05-0.02).

Graph 24 shows also that of the six 'Control' town prevalences, two are placed on the diagonal, two below and two above the line indicating no change between the two surveys. Of the six points corresponding to the 'Treatment' town prevalences, two are below the diagonal and four above suggesting an increase in tuberculin sensitivity.

The mean percentage of reactors among small children in 1959 in the 6 'Treatment' towns was 15.68% and in the other 6 towns 13.92%; the difference of 1.76% is insignificant. It suggests that there was no obvious difference in the degree of tuberculin skin sensitivity between the two groups of towns at the start of the present Investigation.

As for a possible change in the percentages of reactors of each group in the interval between the two surveys, there was an increase in the 'Treatment' group from 15.68% in 1959 to 18.2% in 1966-69 (Table LIII) whereas there was no change in the 'Control' group, the mean percentages of reactors being 13.92 and 13.65% respectively. The differences of 2.52% observed in the 'Treatment' group is not statistically significant but a chi-square test showed P = 0.07.

The findings suggest that the difference in prevalence of tuberculin reactors among small children in the two groups observed in 1966-69 is not likely to be due to any difference existing already in 1959 when the present Investigation was started, but it might have arisen during the period of the Investigation. The possible significance of this observation is discussed in next part of the Report.

XV. GENERAL DISCUSSION

Before drawing the main conclusions, it may be well to recall the aim and purpose of the Investigation. Being impressed with the results obtained by the Tuberculosis Chemotherapy Centre (T.C.C.), Madras, by home treatment in converting 84.1% of advanced bacillary cases of pulmonary tuberculosis to sputum-negative cases - a result comparable to that (92.6%) obtained by one year's treatment in hospital of a similar groups of patients, the present experiment was designed to try out home treatment under ordinary working conditions in India and to see whether it would be possible to render a high majority of all the existing bacillary cases sputum-negative within a year. If as much as 90% of such patients could really be rendered non-infectious in a year, it would be common sense to expect that a major blow would have been dealt to the scourge of tuberculosis. Repeated prevalence surveys should therefore reveal significant decreases in the prevalence

of the disease, and after some time the annual incidence should also come down.

In paying attention to "ordinary working conditions", it was stipulated that the introduction of domiciliary drug therapy should be carried out within a reasonable limit of expenditure which should not be more than could reasonably be expected of Government tuberculosis clinics. Further, attention should be paid to the fact that Government tuberculosis clinics were equipped with limited facilities for diagnosis and in particular that they would not have access to laboratories with facilities for isolation of tubercle bacilli by culture and access to carrying out drug sensitivity tests. At the same time the designers of the experiment were aware that the scientific facilities available at the Madanapalle Centre with its mobile X-ray units and highly developed laboratory, would be suited to maintain a close observation on the developments of the experiment, keeping accurate records and not least should be able to benefit from the prestige earned by the mother institution (the Union Mission Tuberculosis Sanatorium) of over 40 years of service to the general public in the area.

As time went on it became clear that the idealistic intentions and high principles could not be wholly maintained. The mere fact that the Research Unit had at its disposal mobile X-ray units with which it was hoped to detect the majority of the existing bacillary cases within a short time and this would include cases which could only be confirmed as bacillary cases because of the access to the isolation of bacilli by culture, were deviations beyond the scope of ordinary Government clinics. Although the teams which issued drugs in the different towns and the technicians handling the X-ray Unit and manning the laboratory were recruited among the local public and had been trained by the Institution itself, the administration and the statistical set-up

were on a higher level than is normally found in Government hospitals and district health centres. Generally speaking, it may be said that the standard of the work was probably better than could be expected from an ordinary Govt. establishment. With regard to the issue of drugs they were given free of charge and strictly within the stipulations drawn up in the Protocol. Although the Research Unit has access to the information gained by the drug sensitivity tests, it did not make use of this information by making changes in the drugs issued as such information would not be available to ordinary Government clinics.

Although as stated earlier the inspiration to the present investigation was derived from the experience of the T.C.C., Madras, it has to be underlined that the present investigation was carried out under conditions which in many ways differed from those available to the T.C.C.. First, there was no selection of cases but everyone having bacilli in the sputum either by microscopy or culture were offered treatment. Second, no distinction was made during the year of treatment according to whether patients had drug-sensitive or drug-resistant bacilli. Third, as the patients lived up to a distance of 160 km. from the Centre, it was not possible to give them the same close supervision as has been possible at Madras, and they were seen only once a fortnight. It was also not possible to carry out regular home visits with checking of the amount of drugs kept in the homes nor checking as a matter of routine the urine for presence of Isoniazid or PAS. Further, it was the policy of the Research Unit not to insist that patients should discard any treatment they might be receiving when they were picked up by the Unit nor did the Unit forbid patients from taking additional drugs if they so wished or were so advised by their local doctors. The contribution to the community made by the Madanapalle Unit was not to replace existing facilities

but to supplement them with whatever special service it could give in terms of free and efficient diagnosis, cheap and - hopefully - effective drug regimens and a reasonably good follow-up service.

It would be a mistake to compare the present investigation with the kind of controlled drug trials carried out by the T.C.C., Madras. This has been an exercise in the practical application of the basic findings of the T.C.C. as well as possible on all types of patients who would carry on their daily life under ordinary conditions.

As for the lessons to be drawn from the present investigation, the most important was the difficulty in obtaining the full co-operation of the patients. Already at the initial stage 10-20% preferred to have treatment from other sources or no treatment at all. Of the 80-90% who accepted the treatment, a number defaulted every month so that at the end of first year only about 65% still continued to take treatment. Even among those who did fetch their drugs at the fortnightly clinics of the Unit, the intake of drugs was often irregular and faulty. The high proportion of patients continuing to excrete Isoniazid-sensitive bacilli at the end of 12 months treatment with both Isoniazid and PAS, indicate the inadequacy of the drug intake.

There are several reasons for the unsatisfactory cooperation and the relatively high rate of defaulters. First, many patients did not wish it to be known that they were afflicted with tuberculosis so they desisted from attending the clinics and also resisted the visits of our staff to their homes. If the jeep belonging to the Research Unit with "M.T.R.U." conspicuously painted on the front stopped at a house, all the beighbours would believe that there was a case of tuberculosis in the house. Secondly, in certain cases agitation against the work of the Unit

was carried out by local medical practitioners who feared they would lose their patients. Third, inspite of repeated explanations and admonitions many patients did not grasp the seriousness of their illness and being tied down by their daily work on which their meagre earnings depended, they could not find time to go to the clinics to get their drugs but would either send a messenger to fetch the drugs or abstain from the drug issues altogether. The fact that the Unit issued the drugs free and the patients had to pay no charge, made some believe that the matter was not of any great importance.

A serious hindrance to the continued trust and confidence in the treatment of the Unit was undoubtedly that many advanced cases failed to respond to the treatment and perished. As time went on, the public lost faith in the treatment offered which of course according to the Protocol had to remain unchanged throughout the period of the Investigation. The attendance at the clinics was therefore gradually reduced as time went on. In some of the six "treatment" towns the people openly resisted the carrying out of the repeated surveys pointing to the failure of saving a number of their sick people with advanced tuberculosis detected during Survey I.

It would be tempting to attribute the decrease in prevalence from Survey I to Survey III to the active treatment programme set in motion in 1960 and carried on till 1968. However, in the design of the experiment was included the six towns designated the "control" towns. The inclusion of the "control" towns in the 1965–68 Survey - the third for the six "treatment" towns and the first full survey for the six "control" towns - has provided a new dimension to the interpretation of the results observed in the six "treatment" towns. Comparing the prevalence observed in the 12 towns at the time of the 1959 Sample Survey with the

results obtained 6-9 years later at Survey III, it was seen that the decrease in prevalence of tuberculosis observed among the six "treatment" towns among cases positive by microscopy was also observed in the six "control" towns.

The increase in the prevalence of cases positive by culture only which was observed in both groups of six towns can be attributed to the change in the culture technique introduced in 1964. The decrease, however, in the prevalence observed among the microscopically positive cases may represent a general decrease of the prevalence of tuberculosis in the part of India where the present investigation has taken place.

The observation that the impact of the treatment programme on the prevalence of tuberculosis in the six towns has been negligible may seem surprising. Taking however, into consideration the response of the public to the different phases of the programme, it is not surprising that the impact should not be more than modest. Assuming a coverage of 90% at the X-ray Survey, and 90% at the bacteriological examination, it would mean that 81% of all the bacillary cases had been detected while nearly 20% remained unknown. If only 80% of the known cases accepted treatment only 65% of the existing cases could benefit from the treatment programme. Recalling that only 50% or so obtained negative sputum after one year of treatment only 32% of all the existing cases had been rendered sputum-negative by the efforts of the Unit. Adding to this the observation that follow-up examinations of such cases for another four years has shown that 31% of those who had obtained negative sputum at the end of the first year had either died or become sputum positive again while 69% had survived and remained sputum-negative 4 years later, the total effect of the treatment programme has been to convert 22% of all the positive cases to

lasting sputum-negative cases. As many of these patients would have turned sputum negative anyway even if the treatment programme had not taken place at all, it is obvious that the impact could not be very great.

When considering the observations regarding the "pool of infectious cases" it was pointed out that the reason for the continued high level of positive cases year by year was due to the carrying over from year to year of a high proportion of patients diagnosed more than a year earlier who should normally have turned sputum negative.within a few months of treatment with effective chemotherapy but now lived on and continued to excrete tubercle bacilli. From 1960 to 1968, the yearly prevalence of proved bacillary cases stood at a level of 5-7 per 1000 - apart from a peak of 8 per 1000 in 1964 when the culture technique was changed. About two-thirds of these cases were due to "old" cases and one-third to "new" cases. The "old" cases consisted of Categories B and C of which Category B was diagnosed in the previous calendar year and, therefore, about 25% of them would not yet have had sufficient time to turn sputum-negative while the 75% ought to have become negative; similarly, the cases in Category C whose treatment was started more than a year earlier, should also have become negative. It is therefore suggested that if the treatment had been truly effective about 80% of all the "old" cases (Categories B + C) ought to have been eliminated as carriers of infectious tuberculosis. So, deducting 80% of these old cases from the total number of TB positives, it can be calculated that the "pool of infectious cases" should have been reduced by half. The remaining "pool" would then have been represented mainly by the fresh "new" cases plus those of Category B who had not had time to turn sputum-negative.

It should be realised that the reduction of "new" cases which may also be designated as "incidence cases", does necessarily take considerable time. First, there should be time to introduce an active treatment programme and give it a chance to function for some time before a sizeable proportion of the bacillary cases can be rendered sputum-negative. Then there must be time for the persons in the community not yet infected to acquire a primary infection, and for this to develop into a demonstrable tuberculous lesion beginning to excrete bacilli. Assuming the decrease of "new" cases as shown in Graph 13 to be genuine (and not due to artificial factors arising from the investigation itself), the fact that the decrease of the incidence appears to have started already at the beginning of the observation period (in 1960 or 1961) suggests that the factors responsible for this decrease must be different from any arising from the present treatment programme. It is, therefore, suggested that the decrease in the incidence may represent a general decrease in the level of tuberculosis owing to many different factors of which, however, the main factor is likely to be that most Indian patients suffering from tuberculosis somehow do find their way to receive some modern chemotherapy.

Even though it was not possible to demonstrate any community effect of the treatment programme may seem surprising, it would not be correct to dismiss domiciliary drug therapy as a method of no importance in the management of tuberculosis in the community. The fact is that there is no other way in a country of the size of India with its 6-700 million population to treat its several millions of patients suffering from tuberculosis. The present investigation suggests, however, that the type of programme entrusted to the Madanapalle Unit and adopted by it, was not effective enough. This may apply to the size of the staff and the type of clinics

set up but more important than anything else, it applies to the type of chemotherapy offered. No real progress is likely to be achieved unless recourse is taken to issue to the public suffering from tuberculosis effective drug regimens which can cater for patients with drug-sensitive as well as drug-resistant bacilli. Drug-resistance is so widespread that the inability to deal with it properly, affects the willingness of the public to cooperate in active programme.

XVI. SUMMARY

In order to test the applicability of domiciliary drug therapy as a tool in the control of tuberculosis an Investigation was set up in 1958 by the Indian Council of Medical Research, the World Health Organisation and the Union Mission Tuberculosis Sanatorium, Arogyavaram (South India). Twelve towns with populations ranging from 6,000-20,000 situated in Andhra Pradesh (8), Karnataka (3) and Tamil Nadu (1), all within 160 km. of Madanapalle (Andhra Pradesh), were selected.

2. A Sample Survey was carried out in 1959 covering 20-25% of the town populations excluding children below the age of 15 years. Three indices were obtained: the prevalence of (i) bacillary pulmonary tuberculosis, (ii) of radiologically positive cases of presumably active pulmonary tuberculosis and (iii) of reactors to tuberculin tests in school children in the two youngest grades. The 12 towns were ranked according to degree of prevalences and divided into two comparable groups of six towns each; the one was designated the 'Treatment' towns and the other the 'Control' towns. During 1960-61, the remaining 75-80% of the populations in the six 'Treatment' towns were surveyed by X-ray examination of their adult populations followed by sputum examinations by microscopy and culture of cases with radiological signs of pulmonary pathology. All proved bacillary cases of tuberculosis were offered treatment at home with Isoniazid and para-aminosalicylic acid (PAS) in 3 and Isoniazid alone in 3 towns. The six 'Control' towns had no further surveys till five years later when they were included in Survey III.

3. Drugs were issued for two weeks at fortnightly clinics over a period of 12 months. Fifteen per cent of the patients offered treatment did not accept. Of those who started treatment, 35% discontinued while 65% continued till the end of the year.

4. Treatment Results: As Government tuberculosis clinics do not oridinarily have facilities for setting up cultures they must rely upon microscopy, so the present material has been divided into two groups according to the method of sputum examination by which bacilli were found initially: sputum positive by microscopy or by culture only. The former group represents generally more advanced cases than those positive by culture only. At the end of the first year the cases initially positive by microscopy obtained "negative sputum" in 47%, "positive sputum" in 41% and 12% had died. The cases initially positive only by culture were negative in 62%, positive in 32% and 6% had died. Considering cases with Isoniazid-sensitive strains: (a) microscopically positive: TB- 53%, TB+ 37% and died 10%, (b) positive by culture only: TB- 63%, TB+ 31% and died 6%. Among patients with strains initially INH-resistant: (a) TB- 23%, TB+ 55% and died 23%, and (b) 46%, 41% and 13% respectively.

5. Treatment results in "two-drugs' and one-drug towns":

In the towns where INH and PAS were issued the results were: TB- 63%, TB+ 29% and died 8%. In the other towns where Isoniazid only was issued the results were 45%, 44% and 11% respectively; the differences between the results in the two groups were statistically significant.

6. Five years' follow-up: Of 1449 cases (treated and untreated) at five years 41% had negative sputum, 18% positive sputum and 40% had died. The prognosis was closely associated with the initial extent of disease: Cases with (i) small lesions: TB- 69%, TB+ 12% and died 19%; (ii) limited lesions: 54%, 22% and 24% respectively; (iii) moderate lesions: 44%, 25% and 32% and (iv) extensive disease: 25%, 17% and 58%.

7. Five years' follow-up according to the sputum status at the end of the first year of treatment: Of those who had obtained negative sputum at 12 months, five years later 66% remained sputum negative, 16% had become sputum positive and 18% had died; of those who had positive sputum at 12 months, five years later 24% had negative sputum, 20% positive sputum and 56% had died.

8. Mortality: Deaths from all causes for the adult population (15 years and more) were 12.8 per 1000 (95% fiducial limits 9.6-16.0). Deaths from tuberculosis were 0.81 per 1000 (95% fiducial limits 0.27-1.35).

9. "Pool of infectious cases": All cases proved to have excreted tubercle bacilli at least once in a calendar year constituted the "pool". Excluding each year those who had died or moved out the Register consisted of all cases who had had or had bacillary tuberculosis. The average findings for the 6 'Treatment' towns at the mid-period of the Investigation stretching from 1960 (or 1961) to 1968 were as follows: Total number of cases on the Register 12.7 per 1000. They were distributed as follows: sputum negative 37.2%, sputum positive 50.3% and "not examined" 12.5%. The TB-positive cases were sub-divided into (a) cases newly admitted 21.7% (b) cases admitted during the previous year 8.6% and (c) casea admitted earlier than the previous year 20.6%. The two groups (b) & (c) correspond to well over half the cases with positive sputum. They are cases who ought to have been sputum negative but remained sputum positive being failure cases to domiciliary drug therapy.

10. Of the sputum positive cases in the 'pool' 62% had INH-sensitive strains and 38% INH-resistant strains. The latter were found mainly in the groups (b) & (c) where they formed 76.3%.

11. The 'pool of infectious cases' in "INH-PAS" and "INH-towns": The sputum-positive cases in the INH-PAS towns consisted of 69% with INH-sensitive and 31% with INH-resistant bacilli. In the INH towns, cases with INH-sensitive strains were found in 55% and cases with INH-resistant strains in 45%.

12. Prevalence surveys: A second full survey of the six 'Treatment' towns was carriedout 1962-64 and a third survey 1965-68. Survey III included also the 6 'Control' towns in which no action had been taken earlier except for the preliminary Sample Survey in 1959.

Results of the prevalence surveys: The prevalences of bacillary cases in the group with sputum microscopically positive were for Surveys I, II and III 6.84, 5.02 and 4.79 per 1000. The decrease from Survey I to Survey II and from Survey I to Survey III were statistically significant. The prevalence of bacillary tuberculosis among the cases with sputum negative by microscopy but positive by culture were 2.41, 4.15 and 4.92 per 1000. The increase in this group is explained by a significant improvement in the culture technique introduced in 1964 during Survey II. The decrease observed among the microscopically positive cases is considered to represent a real decrease and not one explainable by technical considerations.

13. Prevalence of cases with INH-sensitive and INH-resistant strains: As for cases with INH-sensitive strains the prevalences were at Survey I, II and III among cases positive by microscopy: 5.51, 2.78 and 3.28 per 1000. The difference between Survey I and Survey II corresponds to a drop of 50% and between Survey I and Survey III of 40%, both statistically significant. With regard to the cases with INH-resistant bacilli the group 'all positives' showed at Surveys I, II and III rates of 1.58, 3.33 and 2.45 per 1000; the increase from Survey I to

survey II of 100% is statistically significant. Therefore, in the 6 'treatment' towns a significant drop in the prevalence of cases with Isoniazid sensitive bacilli occurred while the cases with Isoniazid resistant bacilli showed a significant increase.

Comparing the prevalences obtained at Survey III in the 6 'Treatment' towns with the prevalences in the 6 'Control' towns, there was a remarkable similarity. With regard to cases with INH-sensitive bacilli the prevalence in the 'Treatment' towns was 7.26 and in the 'Control' towns 7.22 per 1000. Among the cases with Isoniazid-resistant bacilli the 'Treatment' towns showed 2.45 and the 'Control' towns 1.82 per 1000 or 35% more INH-resistant cases in the 'Treatment' than in the 'Control' towns, but the difference is not statistically significant.

14. As all 12 towns had been surveyed in 1959 and again in 1965-68 it was possible to compare the mean changes in prevalence from 1959 to the 1965-68 survey in the 'treatment' and 'control' groups. Both showed a decrease among the cases which had been positive by microscopy, the difference between the two decreases being insignificant. There was also no significant difference between the mean changes among the cases which had been negative by microscopy but positive by culture.

15. From a comparison of the prevalence of bacillary tuberculosis as found by the X-ray surveys and the known cases on the Register it was estimated that about one-third of the existing bacillary cases in the community were unknown to the Centre (Research Unit).

16. A tuberculin sample survey was carried out in the 12 towns in 1966-69. In the age group 2-4 years the mean percentage of reactors in the 'treatment' towns was 9.60 and in the 'control' towns 4.49. In age group 5-9 it was 18.21 and 13.85%

respectively. As there was no difference between the reactors among young school children in the two groups in the 1959 Sample Survey, the observations suggest a greater risk of infection in the 'treatment' towns than in the 'control' towns since 1959.

17. It is concluded that although there is evidence of a decrease in the prevalence of cases with Isoniazid sensitive bacilli and an increase of cases with Isoniazid resistant bacilli, particularly in the towns where the treatment consisted only of Isoniazid, the effect of the active case finding and treatment programme has not been able to produce any measurable change in prevalence between the 'treatment' group and the 'control' group except possibly for a greater risk of infection as shown in a higher percentage of tuberculin reactors among small children in the 'treatment' towns than in the 'control' towns. The relatively unsatisfactory cooperation on part of the patients in accepting the treatment, the limited effect of the drug regimens offered and the relatively short time allowed for the effect of the treatment programme to influence the prevalence and incidence may be reasons for the absence of any clear difference between the 'treatment' and 'control' towns. The observation of a decrease in prevalence of tuberculosis among cases positive by microscopy is thought to reflect a general decrease of the prevalence of tuberculosis in the community.

XVII. ACKNOWLEDGEMENT

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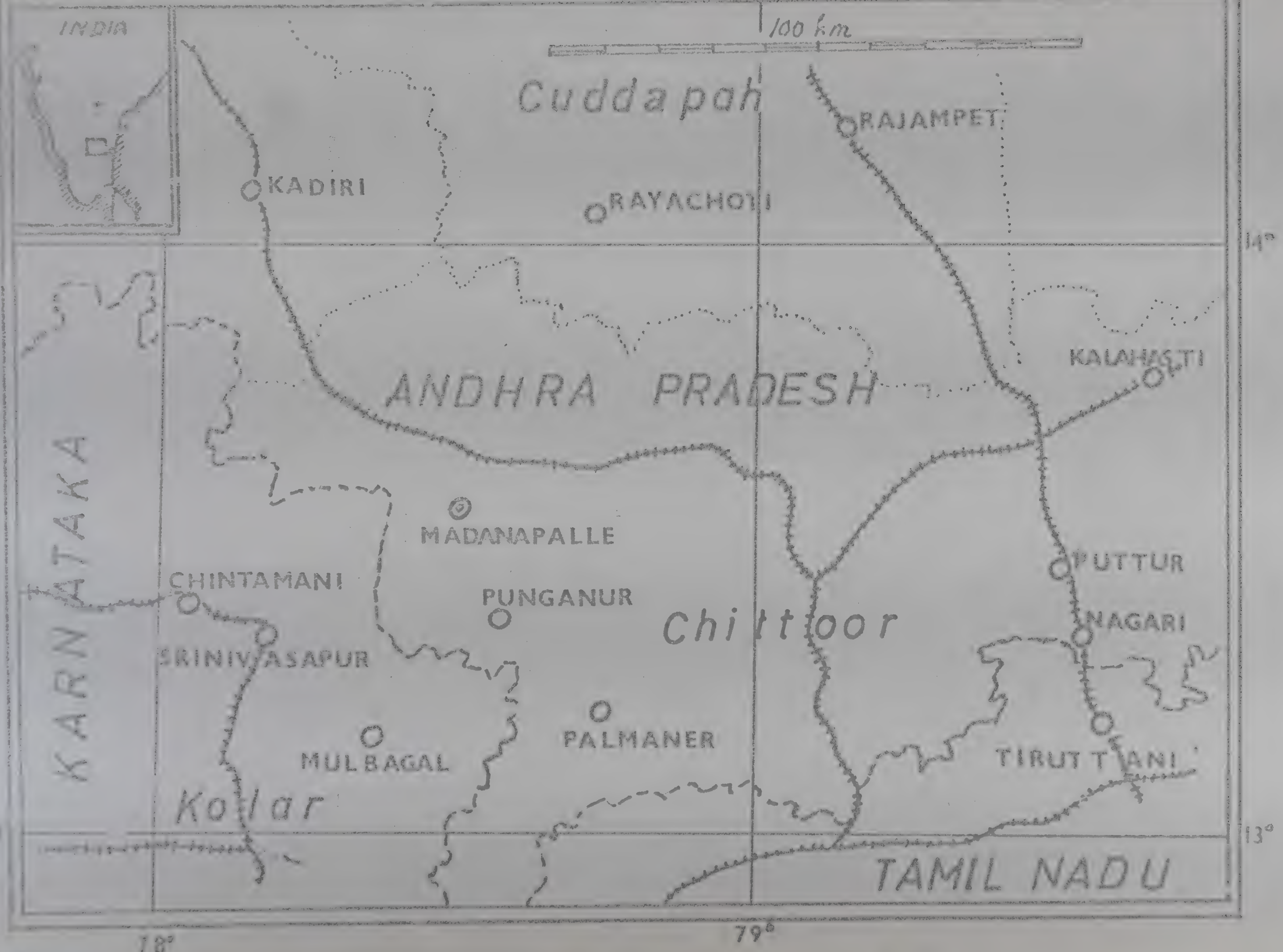
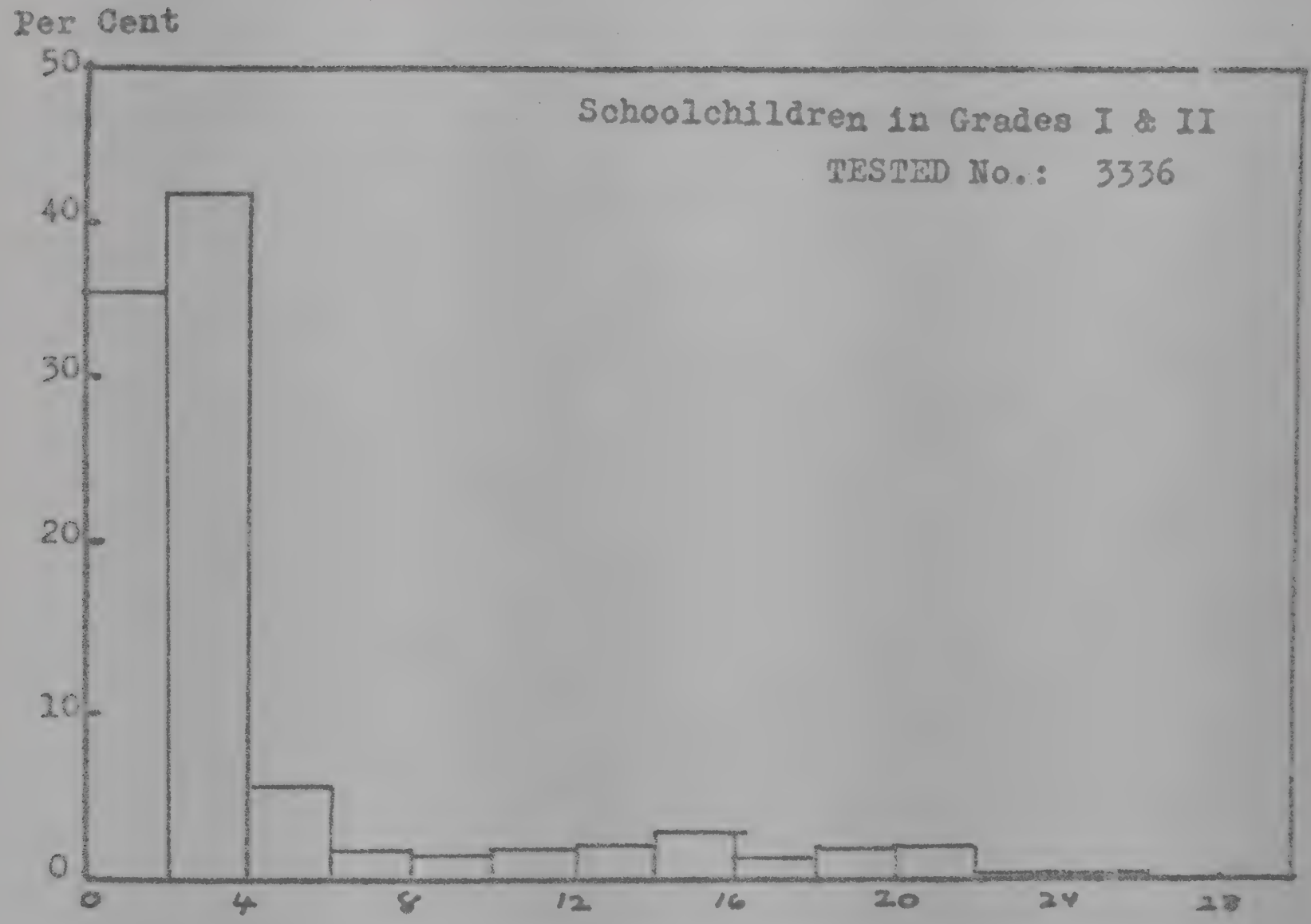
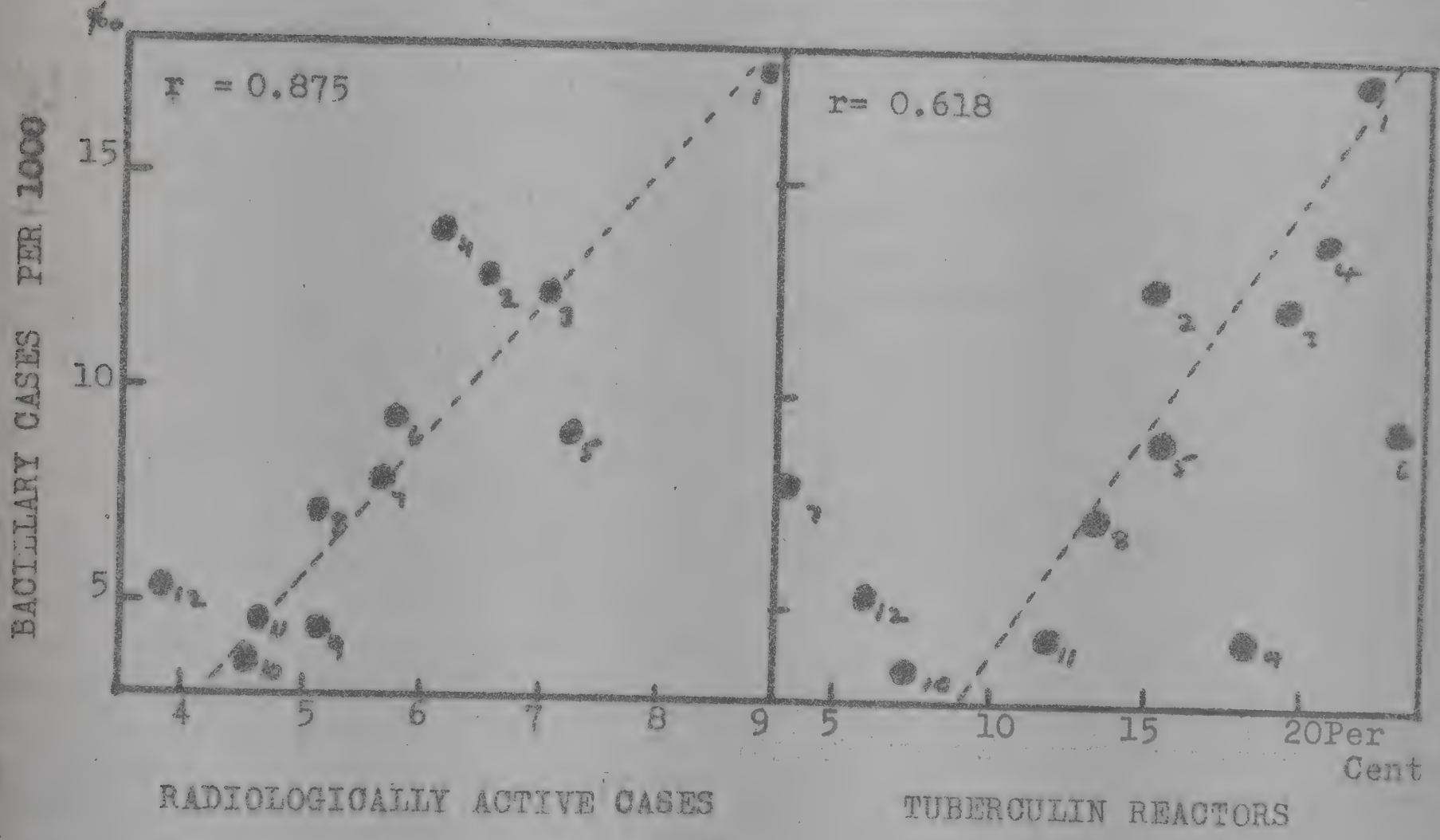

INDIA
100 km
Cuddapah
KADIRI
RAYACHOTI
RAJAMPET
KALAHASTI
ANDHRA PRADESH
KARNATAKA
MADANAPALLE
CHINTAMANI
PUNGANUR
Chittoor
PUTTUR
NAGARI
SRINIVASAPUR
PALMANER
MULBAGAL
TIRUTTANI
Kolar
TAMIL NADU
14°
13°
12°
78°
79°

Figure 1.


Per Cent
50
40
30
20
10
0
Schoolchildren in Grades I & II
TESTED No.: 3336
0
4
8
12
16
20
24
28
Diameter of Indurations in Millimeters
1959 SAMPLE SURVEY

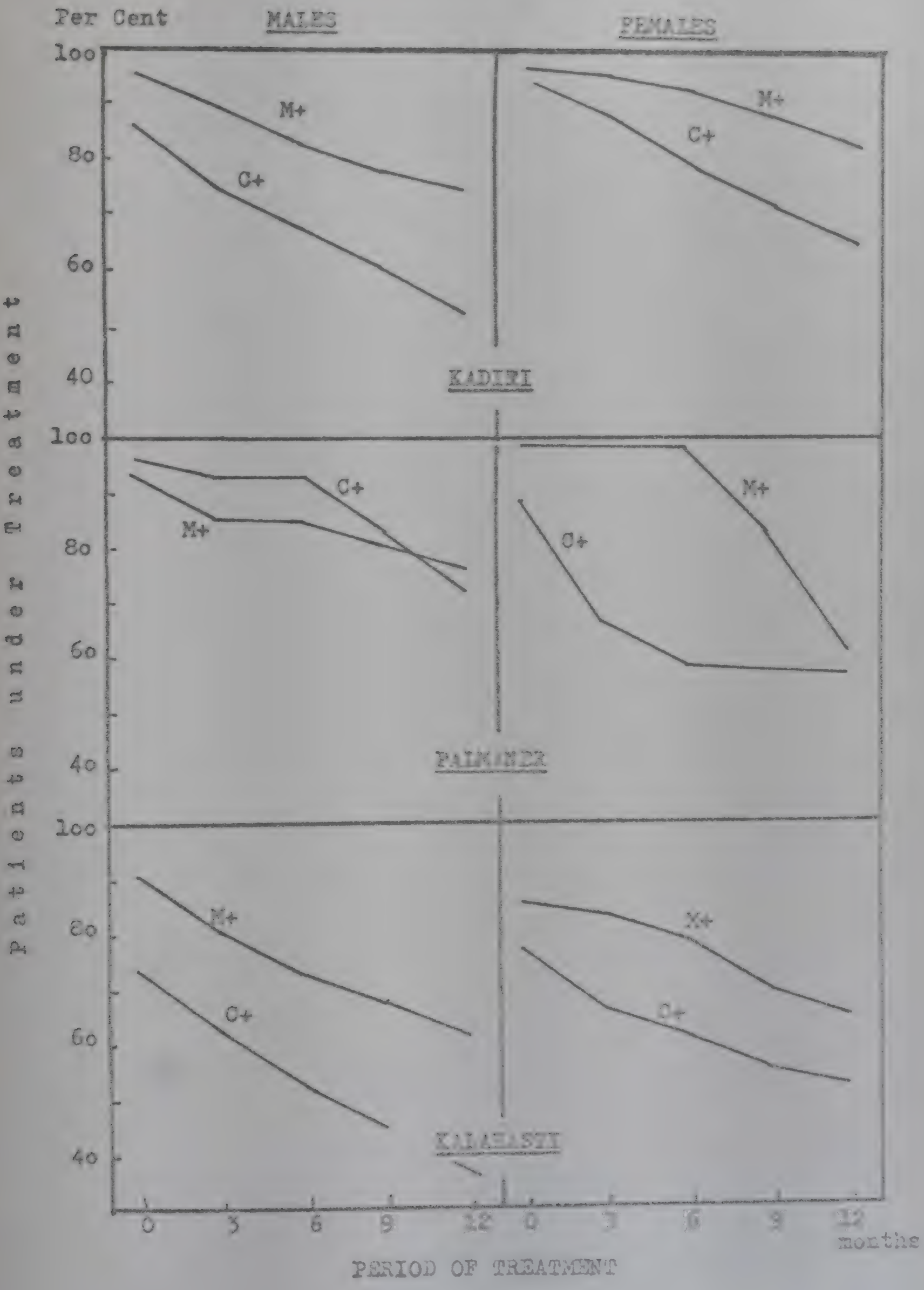
Graph 1.

1959 Sample Survey

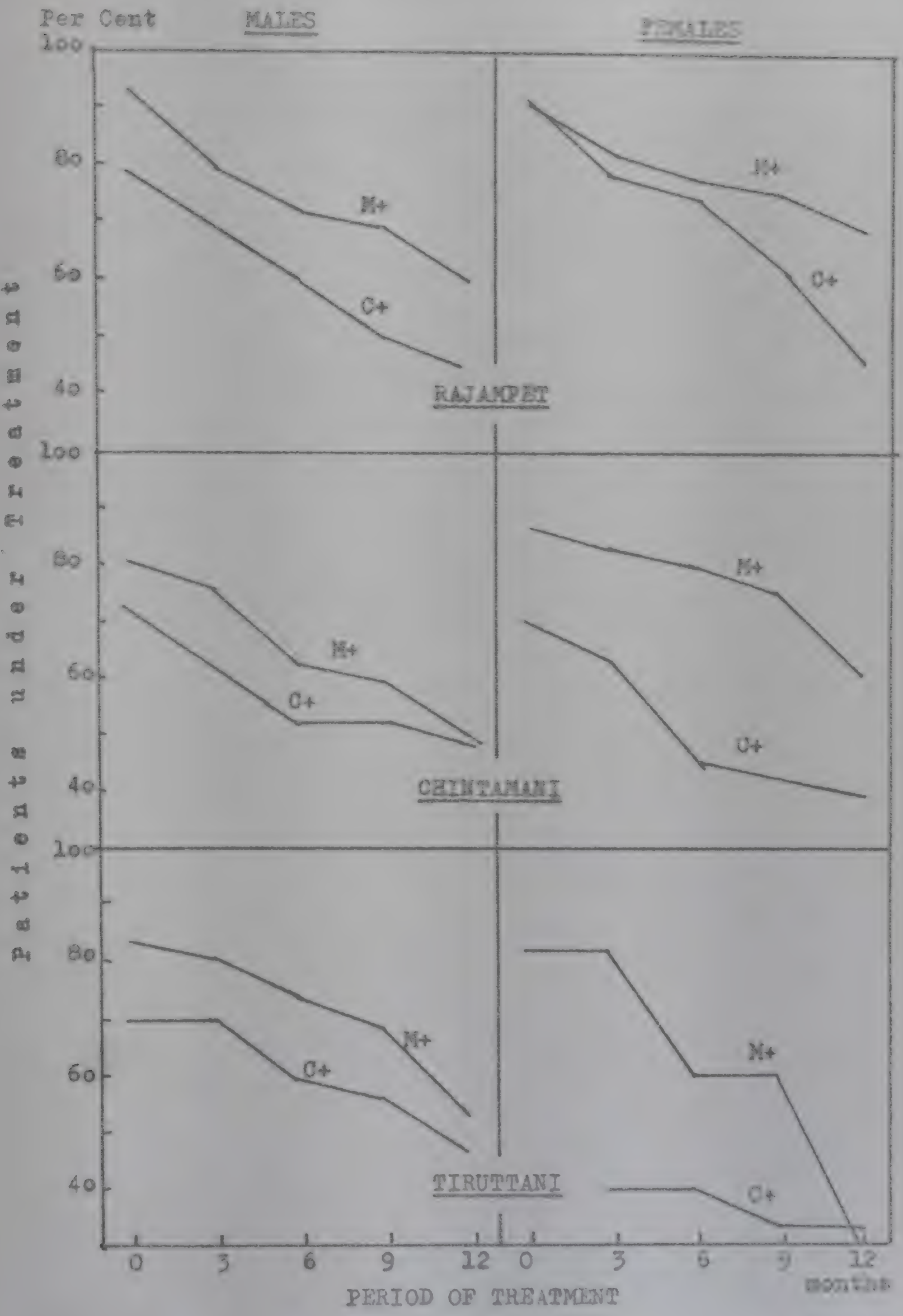


Graph 2.

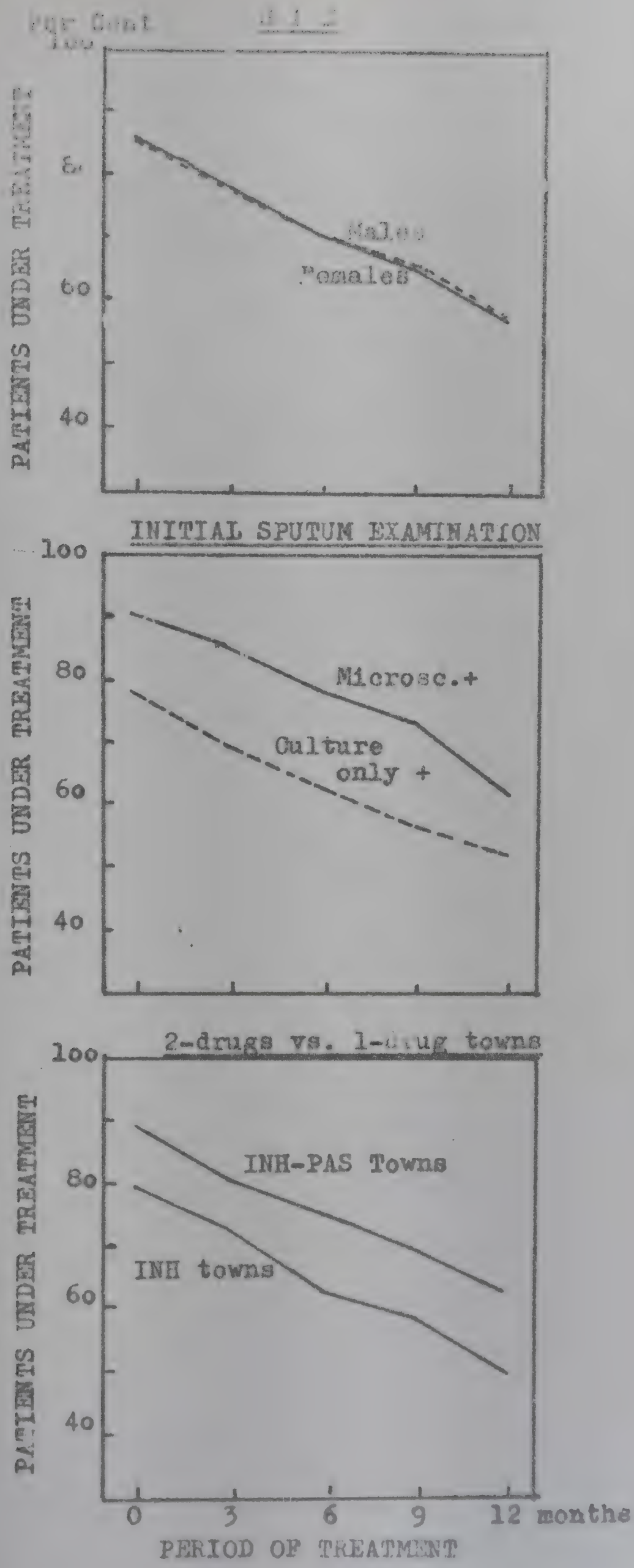
Correlations between the prevalence of bacillary cases per 1000 and (i) the percentage of radiologically active cases and (ii) the percentage of tuberculin reactors.- The numbers indicate the rank of the 12 towns as shown on p.26.


Per Cent
MALES
FEMALES
100
80
60
40
M+
C+
KADIRI
PALKONDA
KALAHASTI
Patients under treatment
0
3
6
9
12
months
PERIOD OF TREATMENT

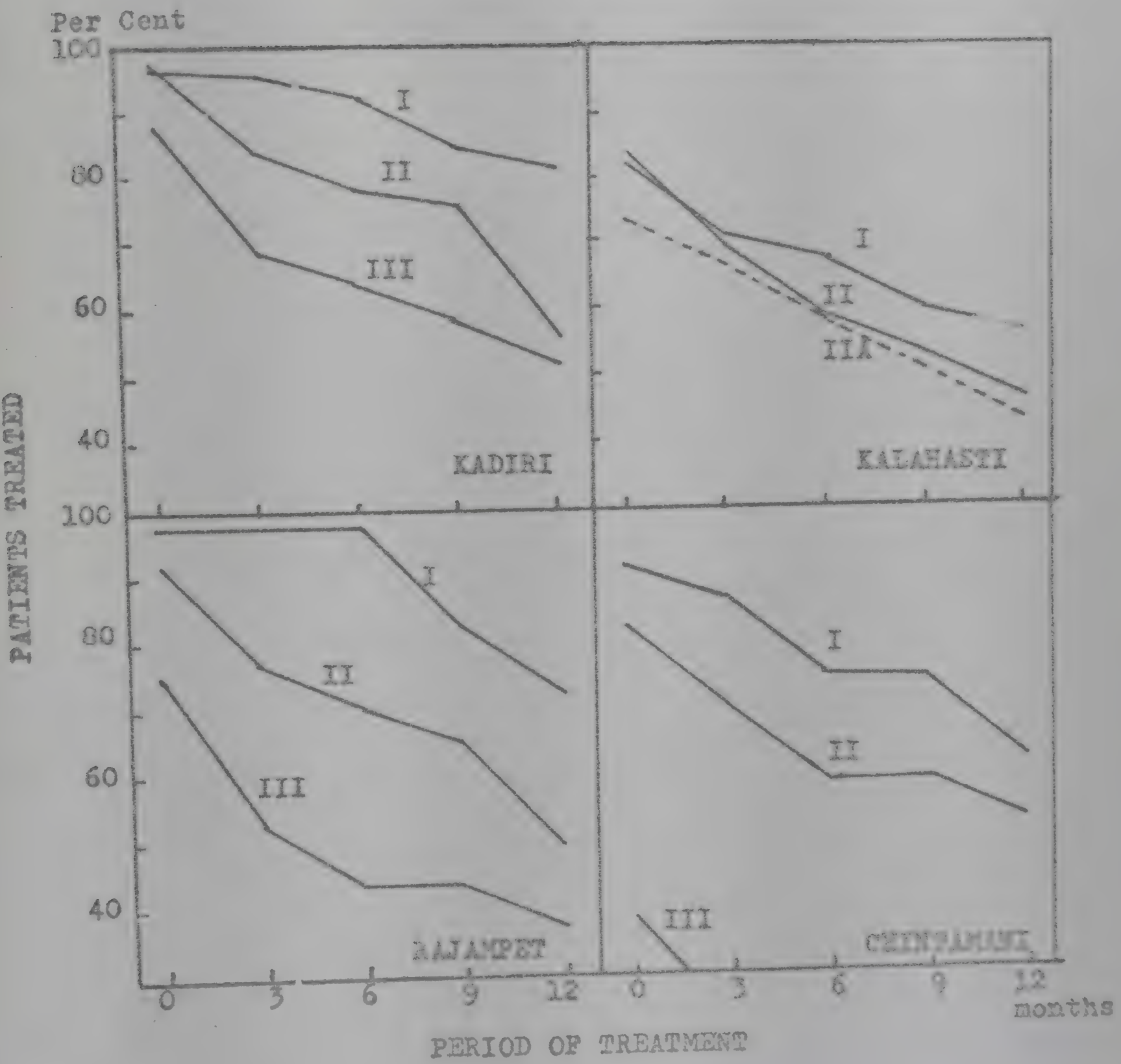
Graph 3.


Per Cent
MALES
FEMALES
100
80
60
40
RAJAMPET
M+
C+
CHINTAMANI
TIRUTTANI
Patients under Treatment
0
3
6
9
12
months
PERIOD OF TREATMENT

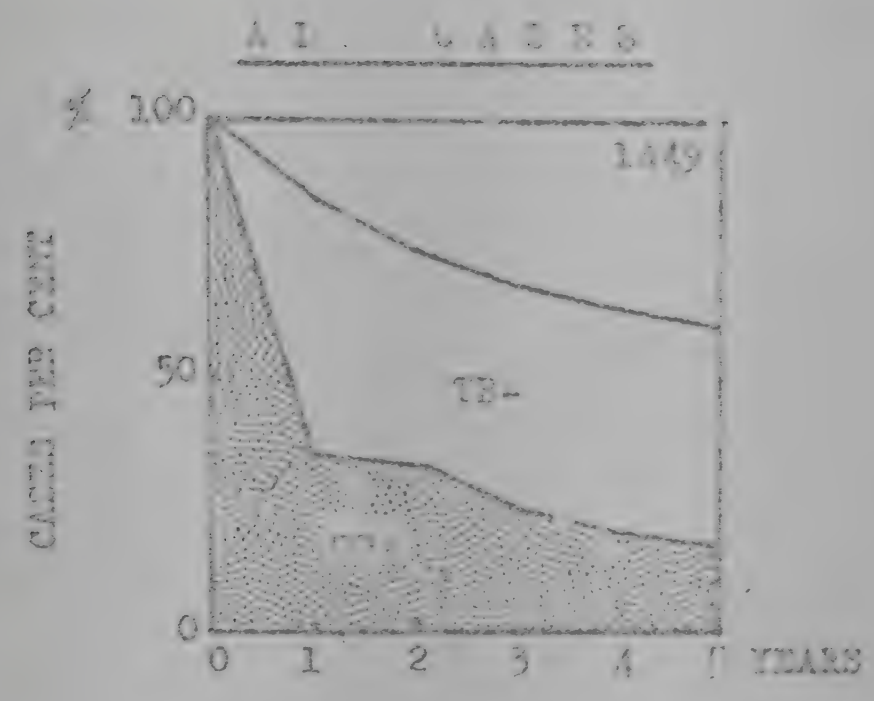
Graph 4.


Per Cent
100
80
60
40
PATIENTS UNDER TREATMENT
Males
Females
INITIAL SPUTUM EXAMINATION
100
80
60
40
PATIENTS UNDER TREATMENT
Microsc.+
Culture only +
2-drugs vs. 1-drug towns
100
80
60
40
PATIENTS UNDER TREATMENT
INH-PAS Towns
INH towns
0
3
6
9
12 months
PERIOD OF TREATMENT

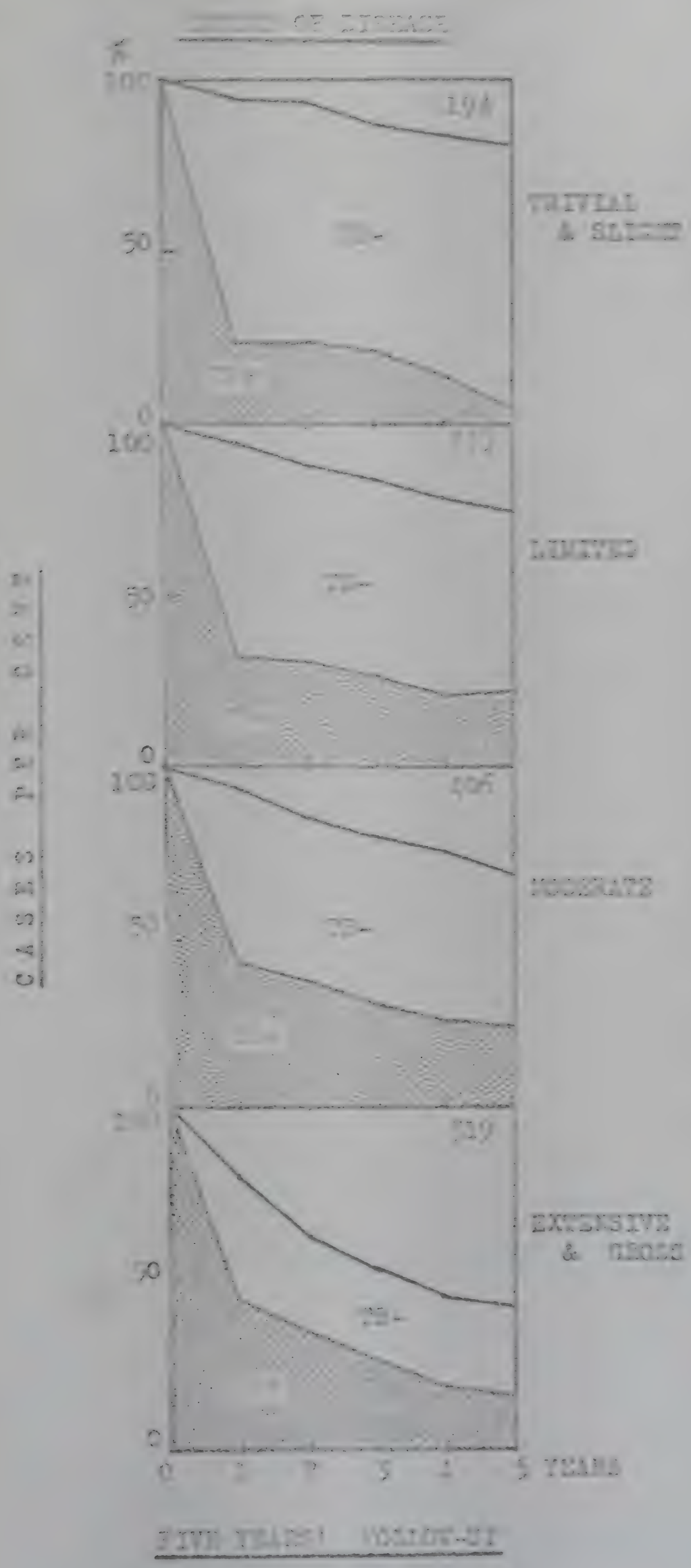
Graph 5.


Per Cent
100
80
60
40
PATIENTS TREATED
KADIRI
KALAHASTI
RAJAMPET
CHINNAMANDEM
I
II
III
0
3
6
9
12
months
PERIOD OF TREATMENT

Graph 6

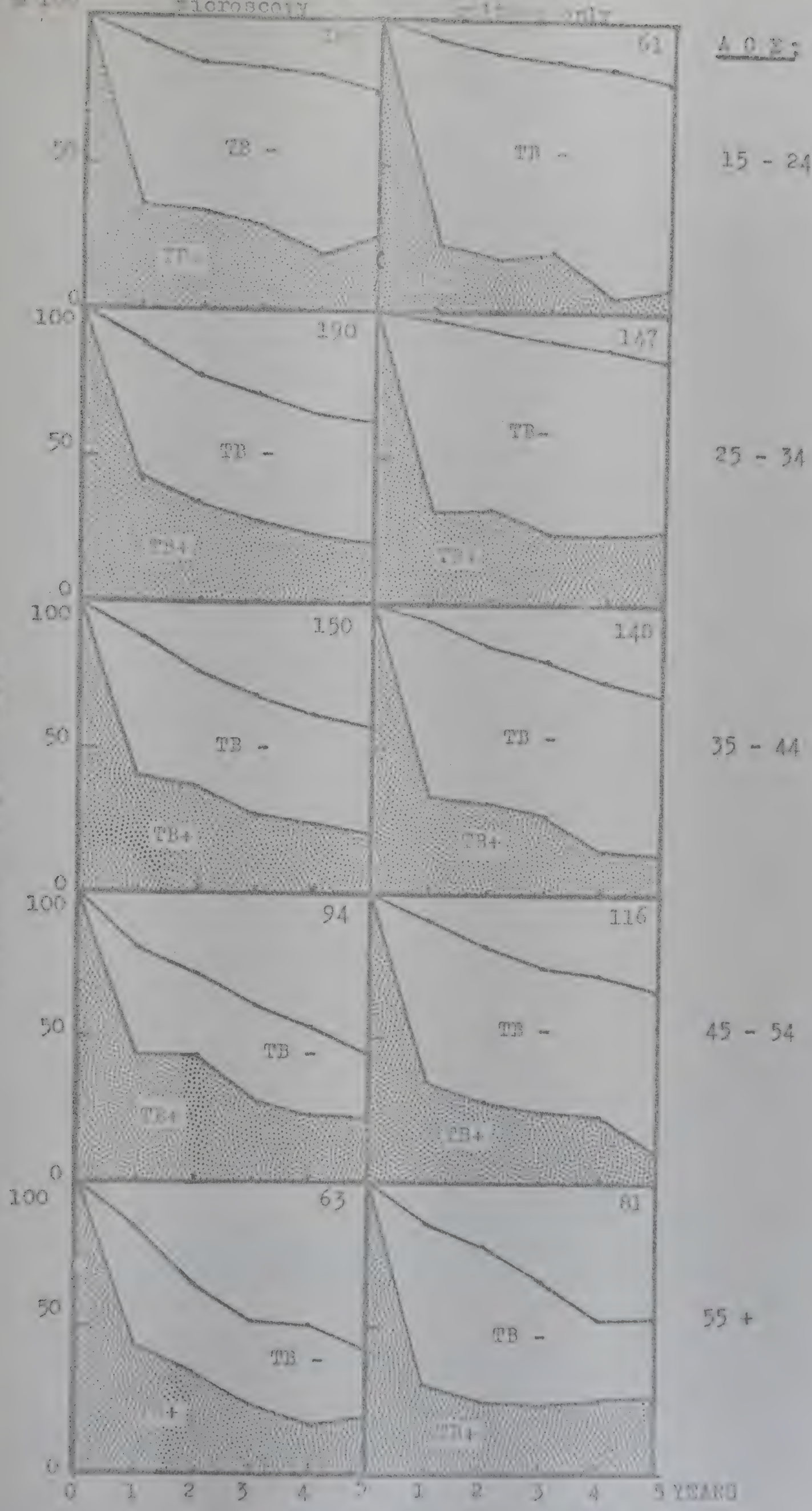

ALL CASES
% 100
50
0
CASES PER CENT
1449
TB+
TB-
0 1 2 3 4 [YEARS
FIVE YEARS' FOLLOW-UP

Graph 7.

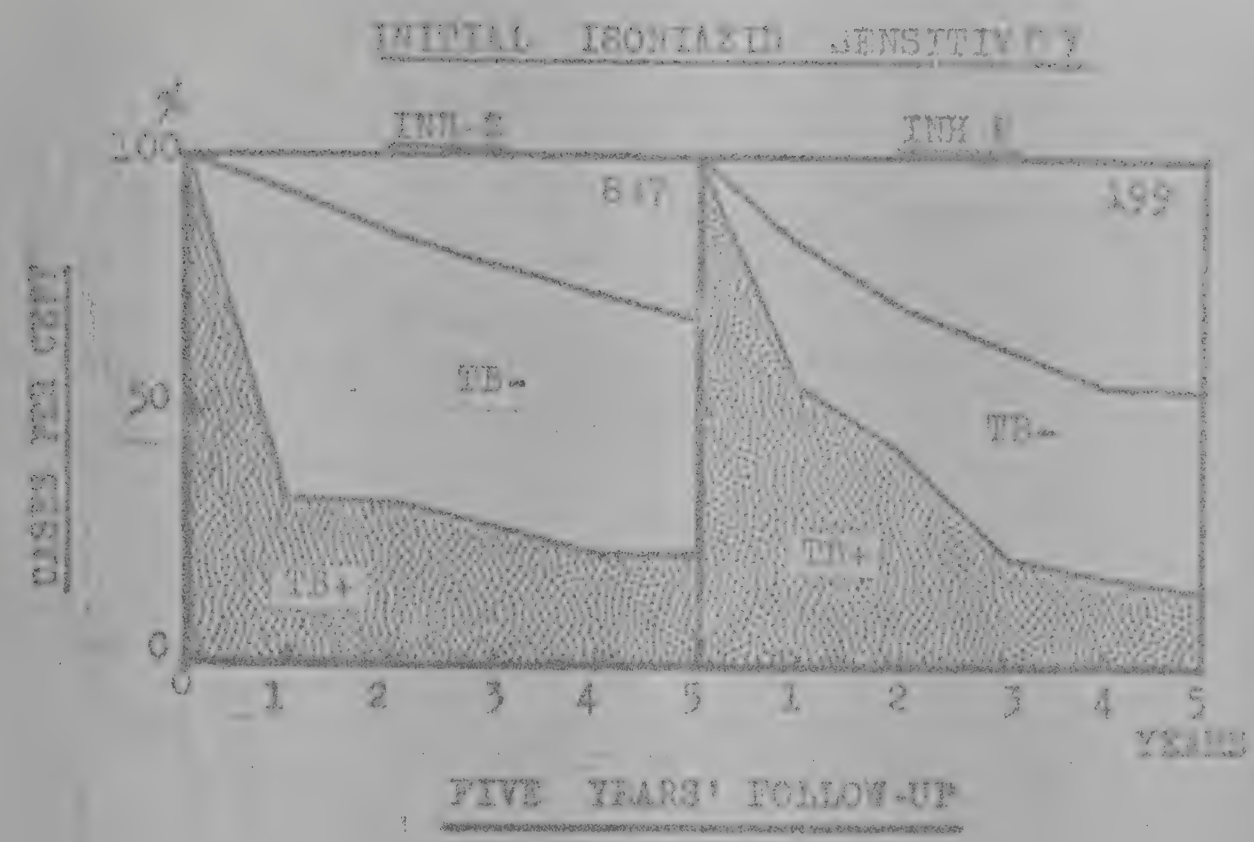

TRIVIAL & SLIGHT
LIMITED
MODERATE
EXTENSIVE & SEVERE
CASES PER 100
0
50
100
150
200
0
1
2
3
4
5 YEARS

Graph 8.

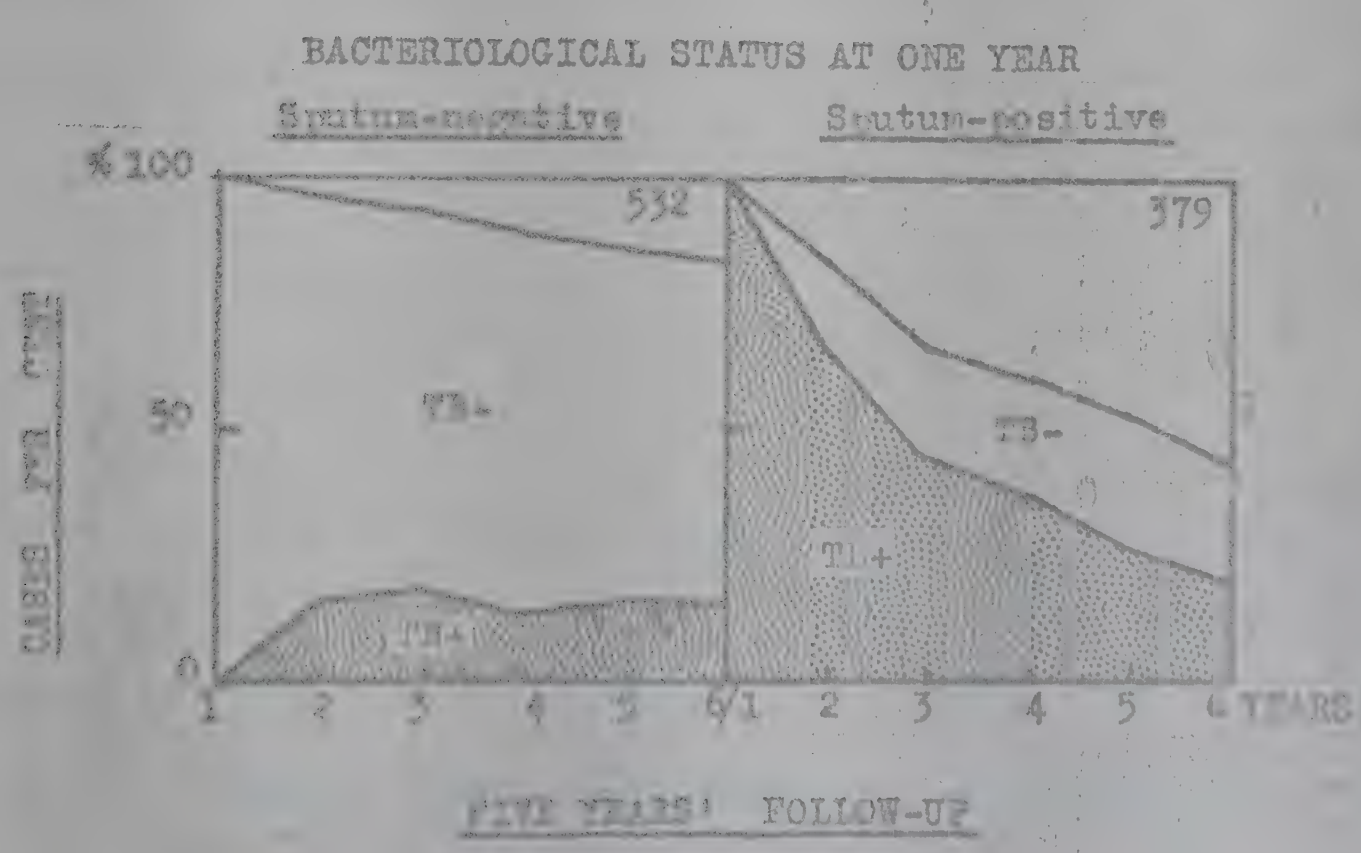
SPUTUM POSITIVE TUBERCULOSIS BY
Microscopy
[illegible] only



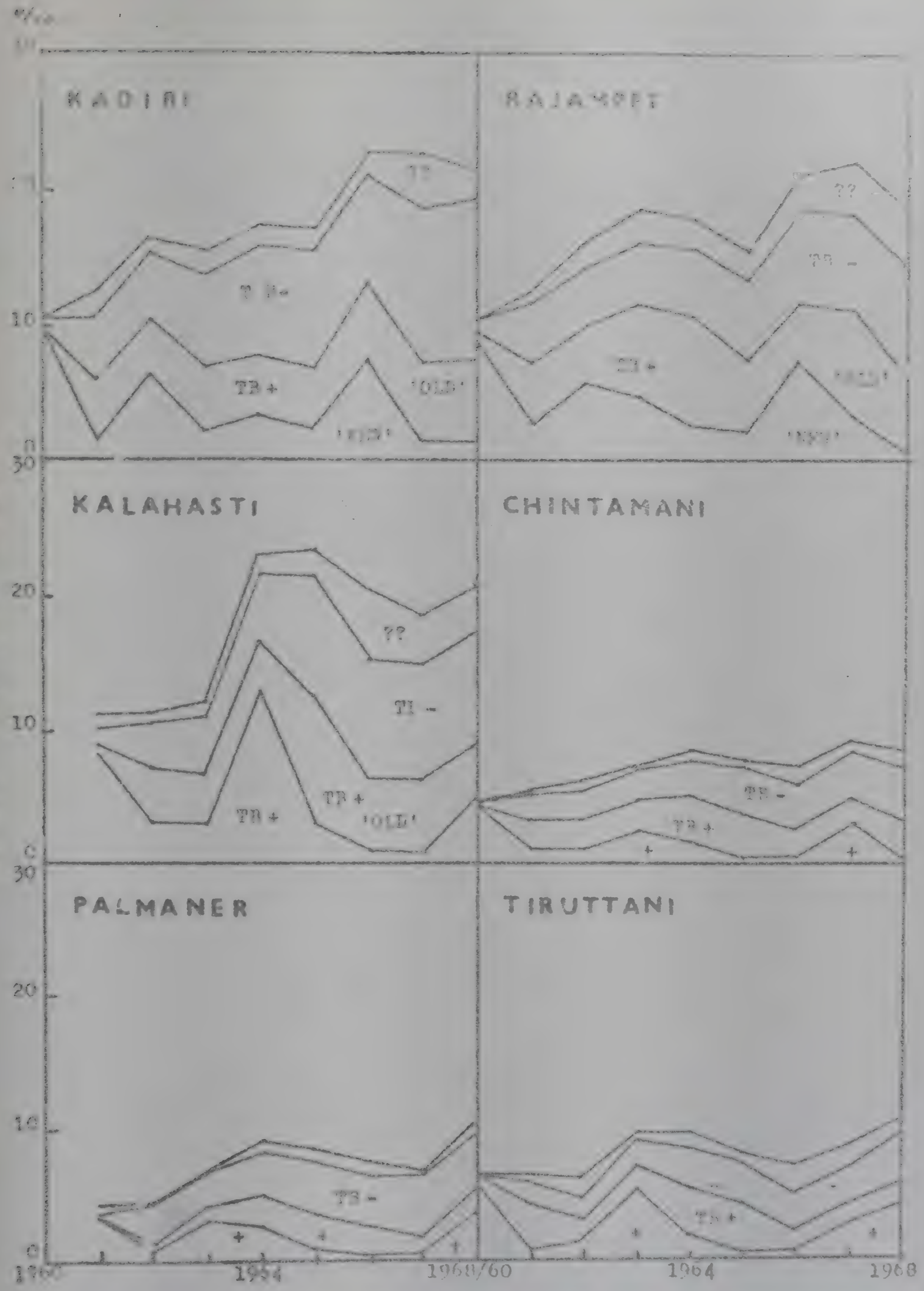
FIVE YEARS FOLLOW-UP



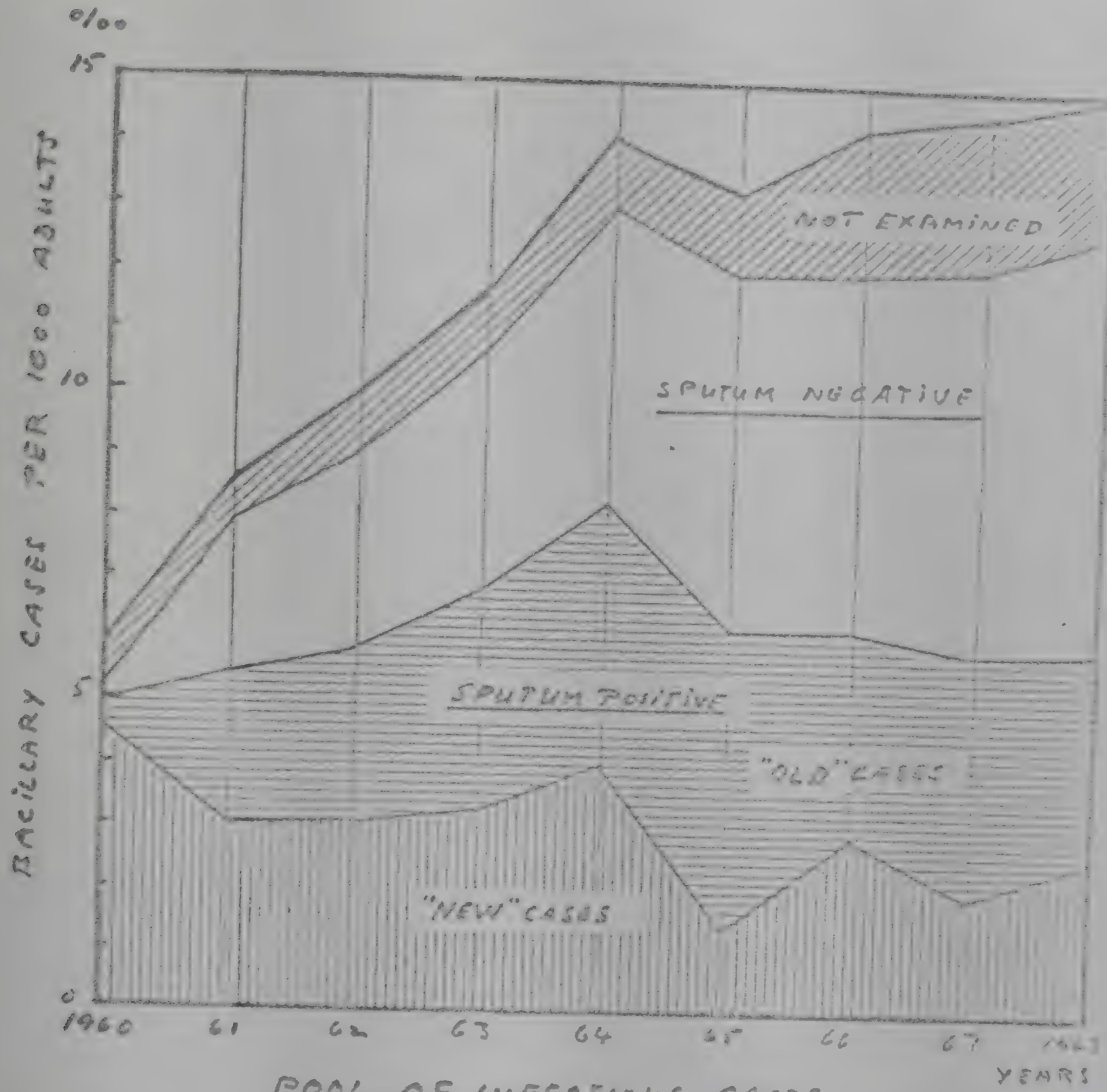
Graph 10



Graph 11.


KADIRI
RAJAMPET
KALAHASTI
CHINTAMANI
PALMANER
TIRUTTANI
TB+
TB-
'OLL'
1954
1960/61
1964
1968
CASES PER 1000 ADULTS
POOL OF INFECTIOUS CASES

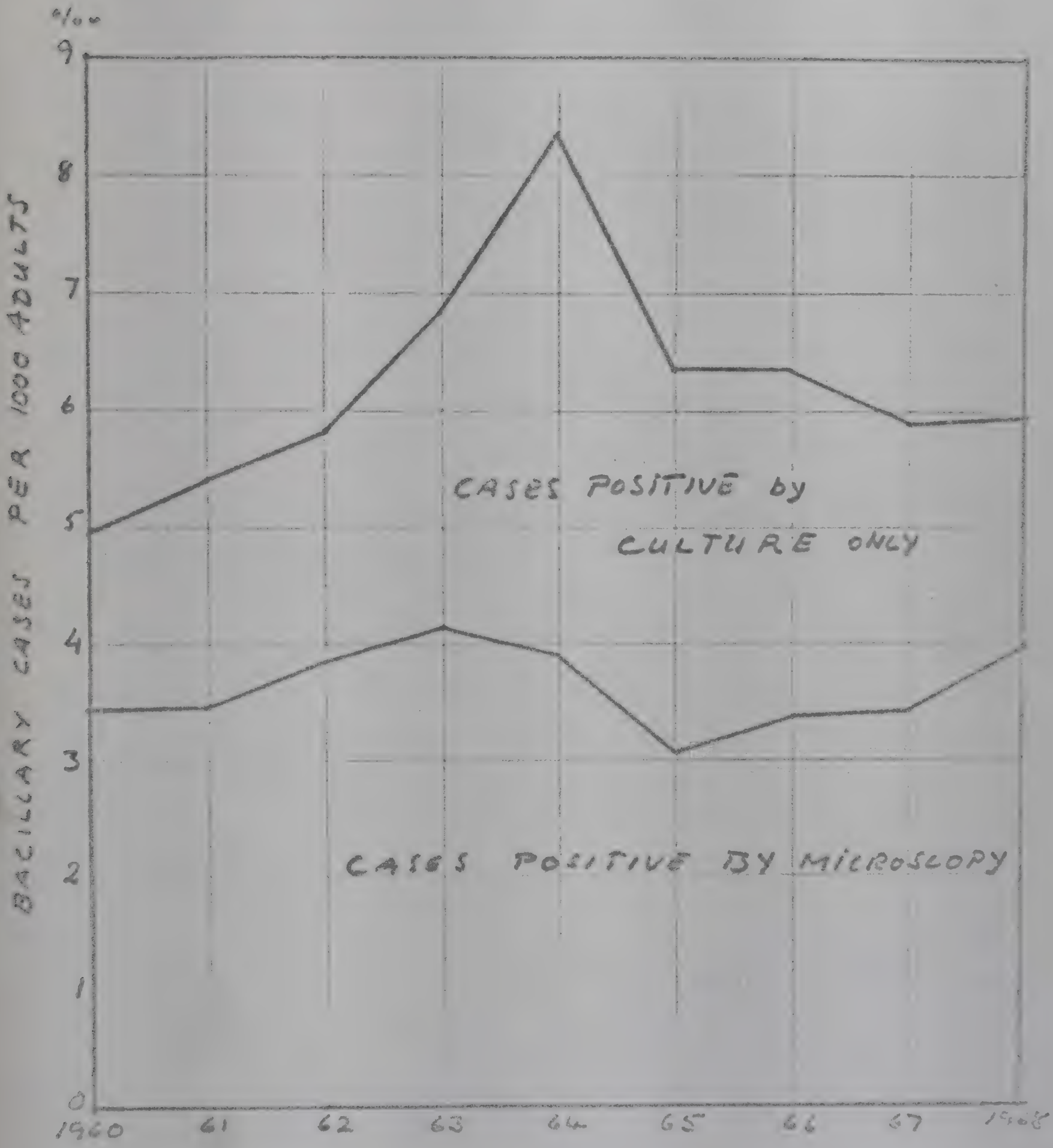
Graph 12.



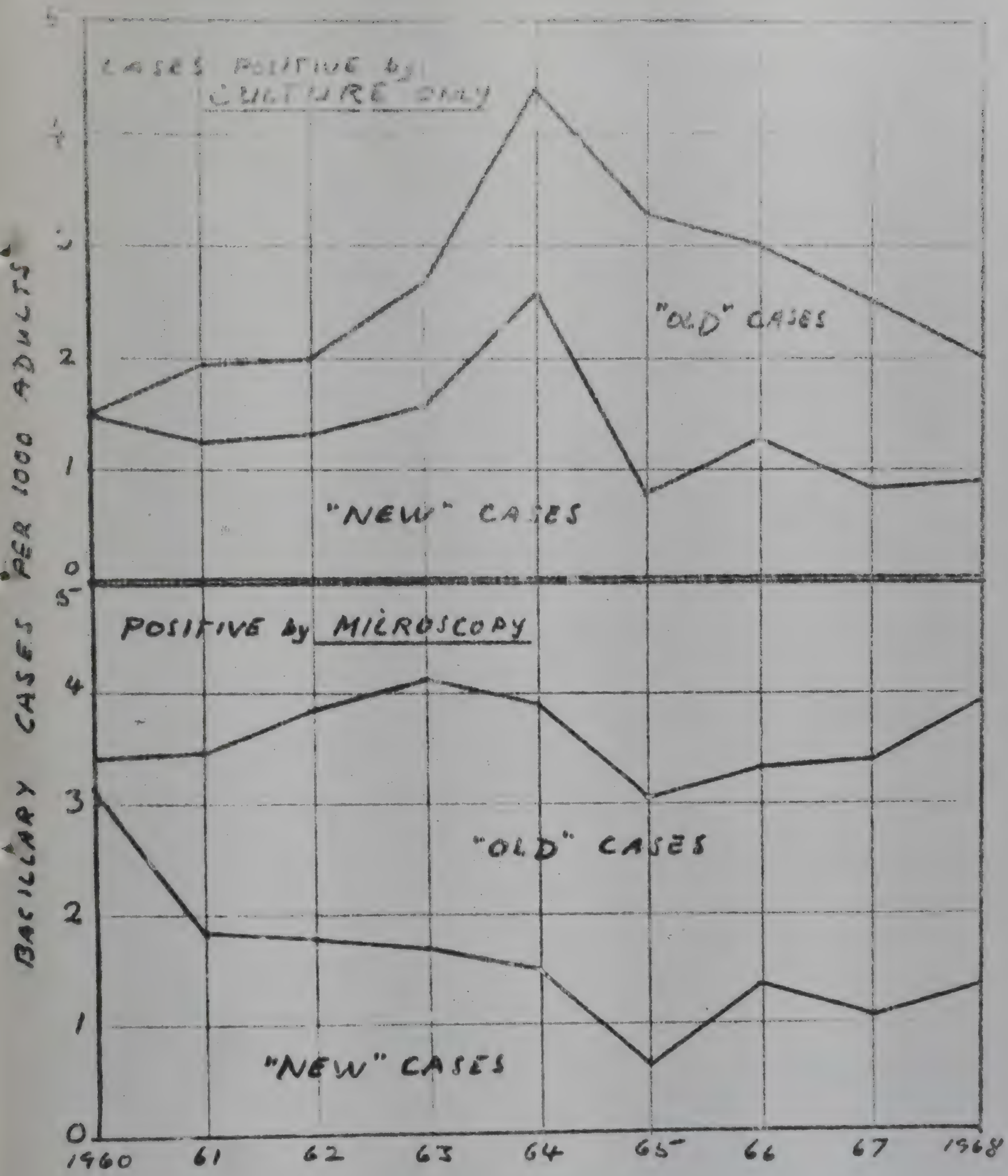
POOL OF INFECTIOUS CASES

MEANS of 6 "Treatment" Towns

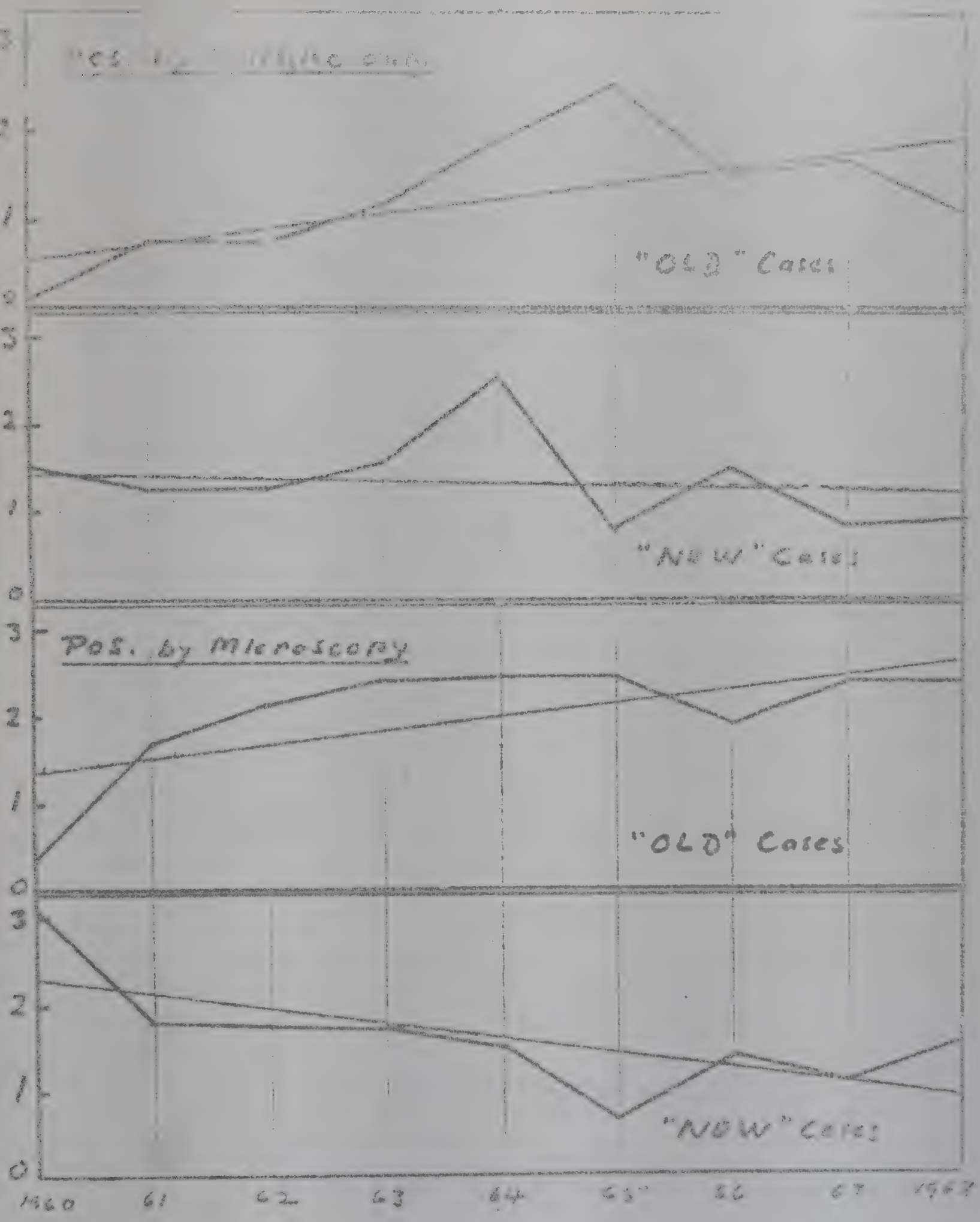
Graph 13.


‰
9
8
7
6
5
4
3
2
1
0
BACILLARY CASES PER 1000 ADULTS
CASES POSITIVE by CULTURE ONLY
CASES POSITIVE BY MICROSCOPY
1960
61
62
63
64
65
66
67
1968
POOL OF INFECTIOUS CASES

Graph 14.

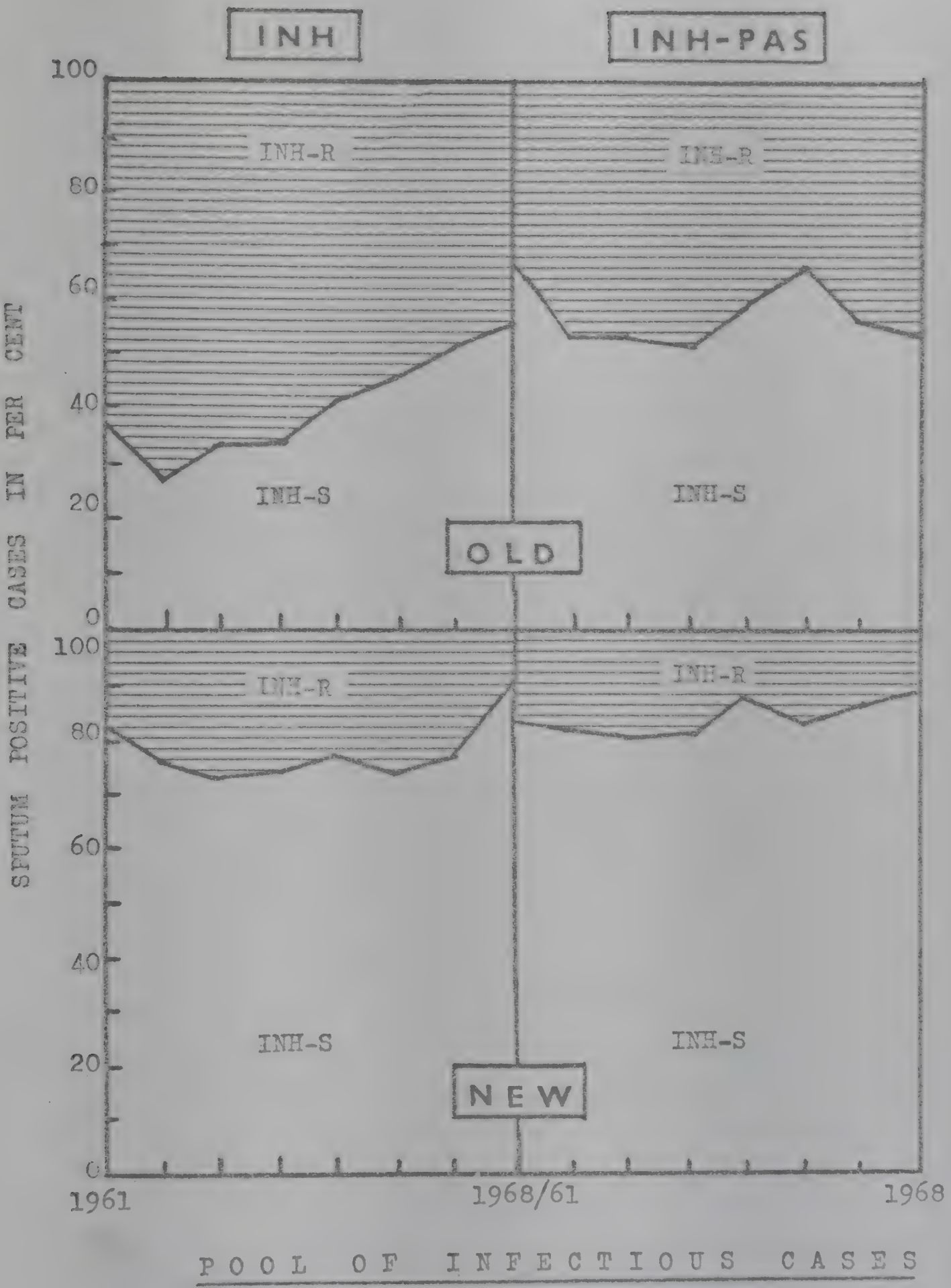

CASES POSITIVE by CULTURE ONLY
"OLD" CASES
"NEW" CASES
POSITIVE by MICROSCOPY
"OLD" CASES
"NEW" CASES
BACILLARY CASES PER 1000 ADULTS
0
1
2
3
4
5
1960
61
62
63
64
65
66
67
1968
POOL OF INFECTIOUS CASES

Graph 15.



POOL OF INFECTIOUS CASES

Graph 16.


INH
INH-PAS
100
80
60
40
20
0
INH-R
INH-S
OLD
NEW
1961
1968/61
1968
SPUTUM POSITIVE CASES IN PER CENT
POOL OF INFECTIOUS CASES

Graph 17.

SURVEY I

SURVEY II

CASES PER 1000

M

F

KADIRI

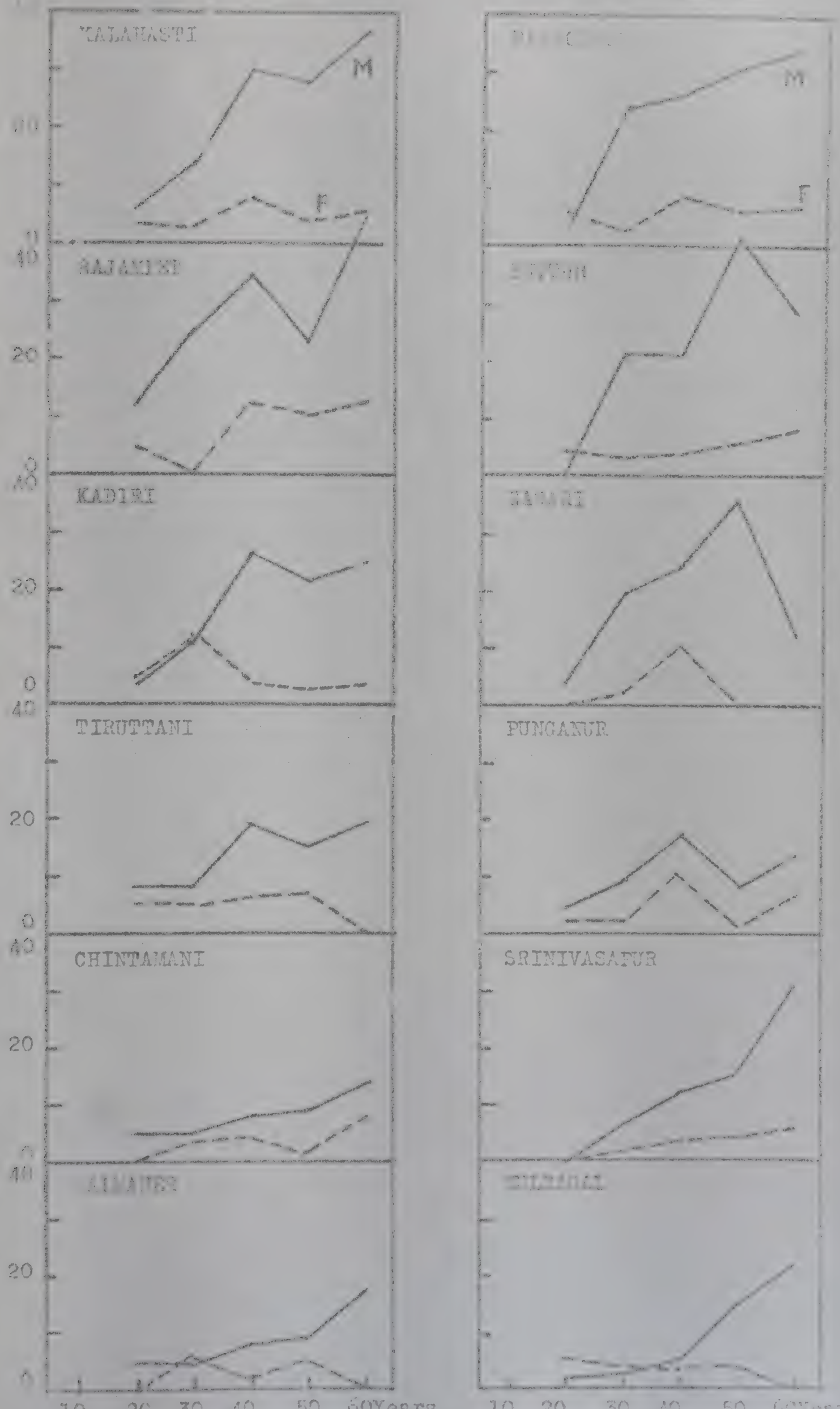
PALMANER

AGE

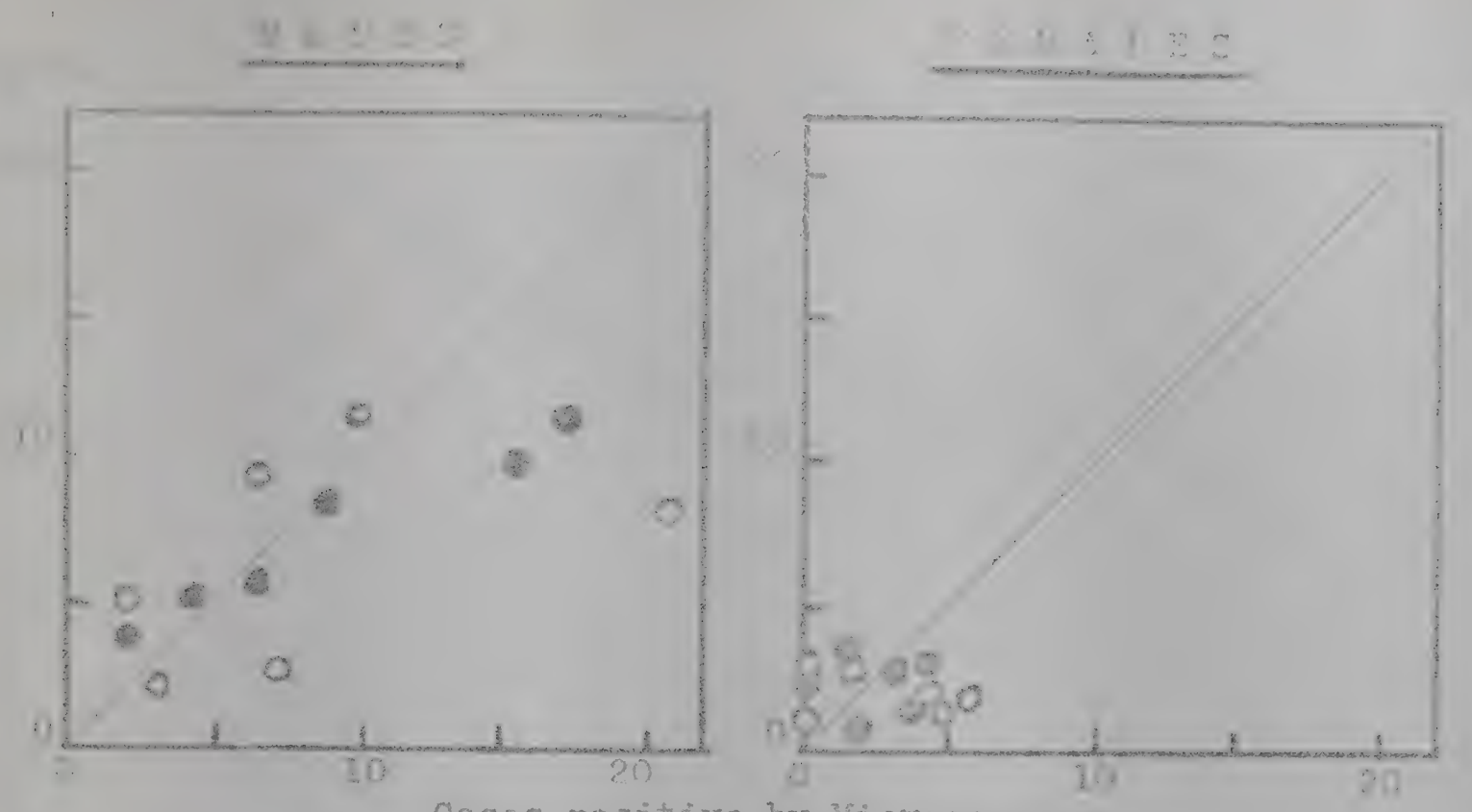
SURVEY III

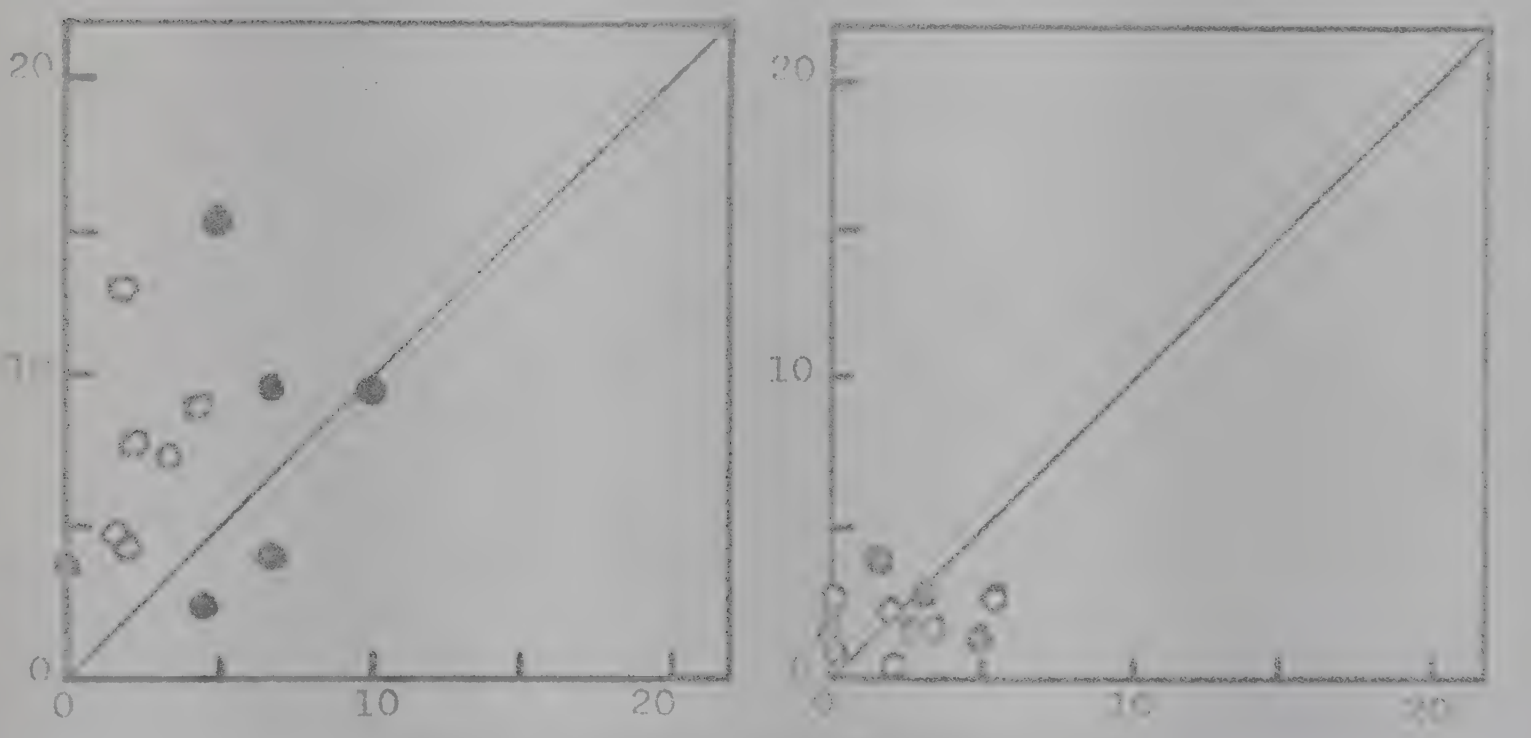
Per 1000 "TREATMENT" Towns

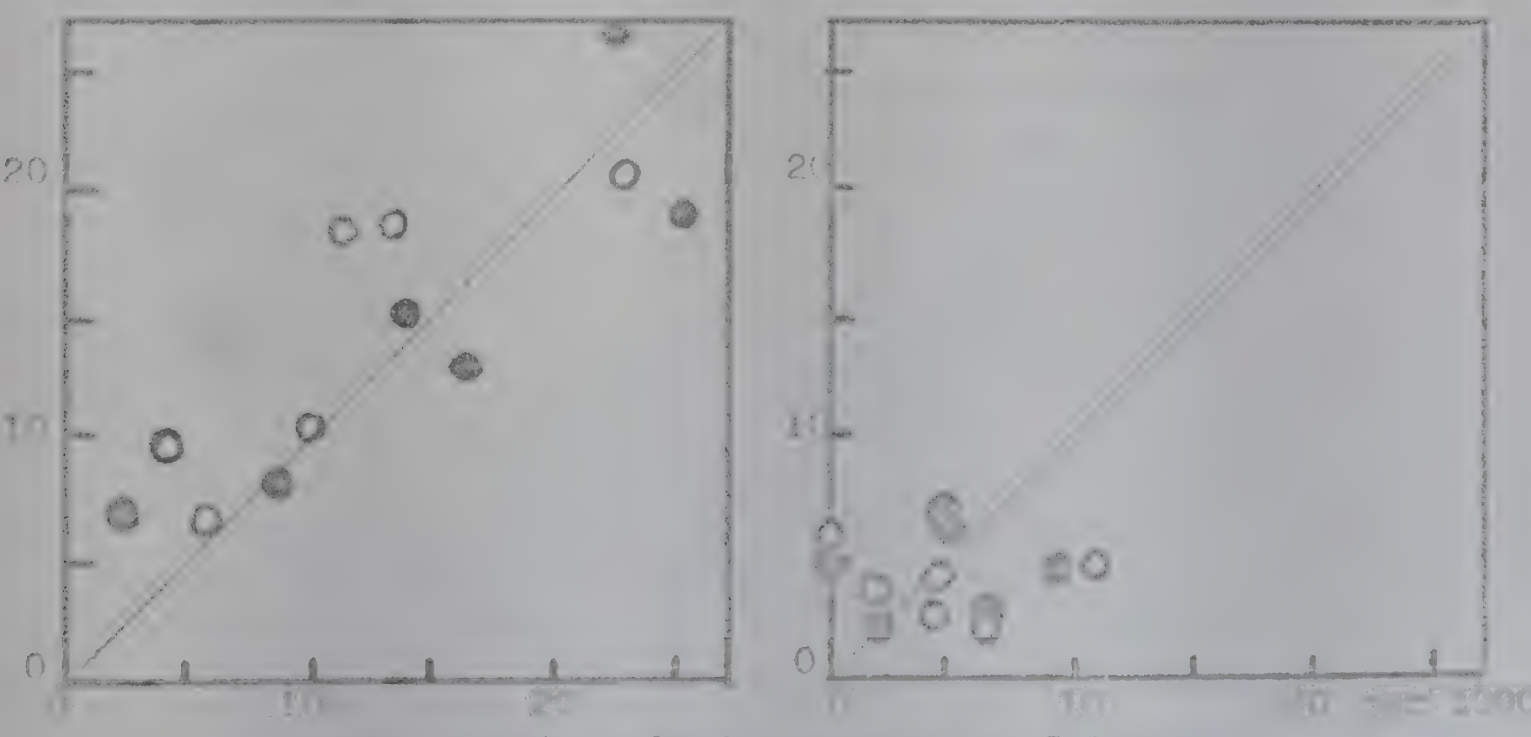
"CONTROL"



CASES PER 1000



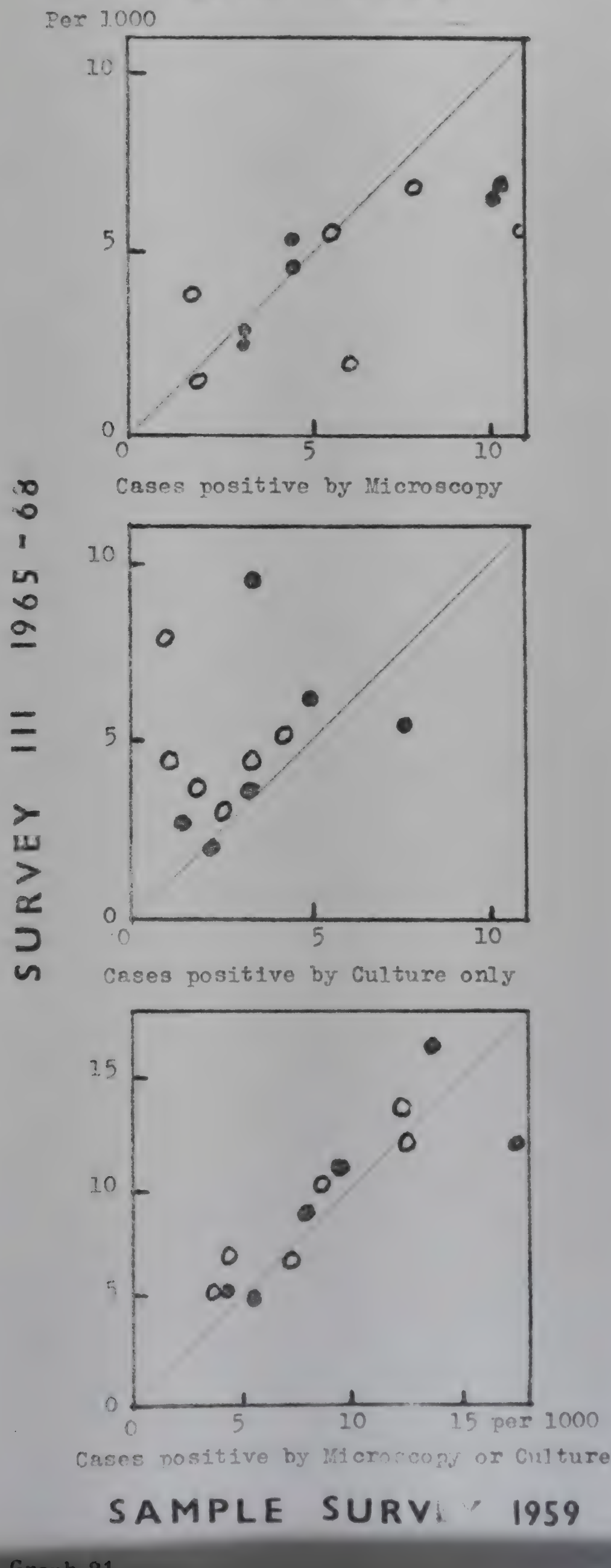




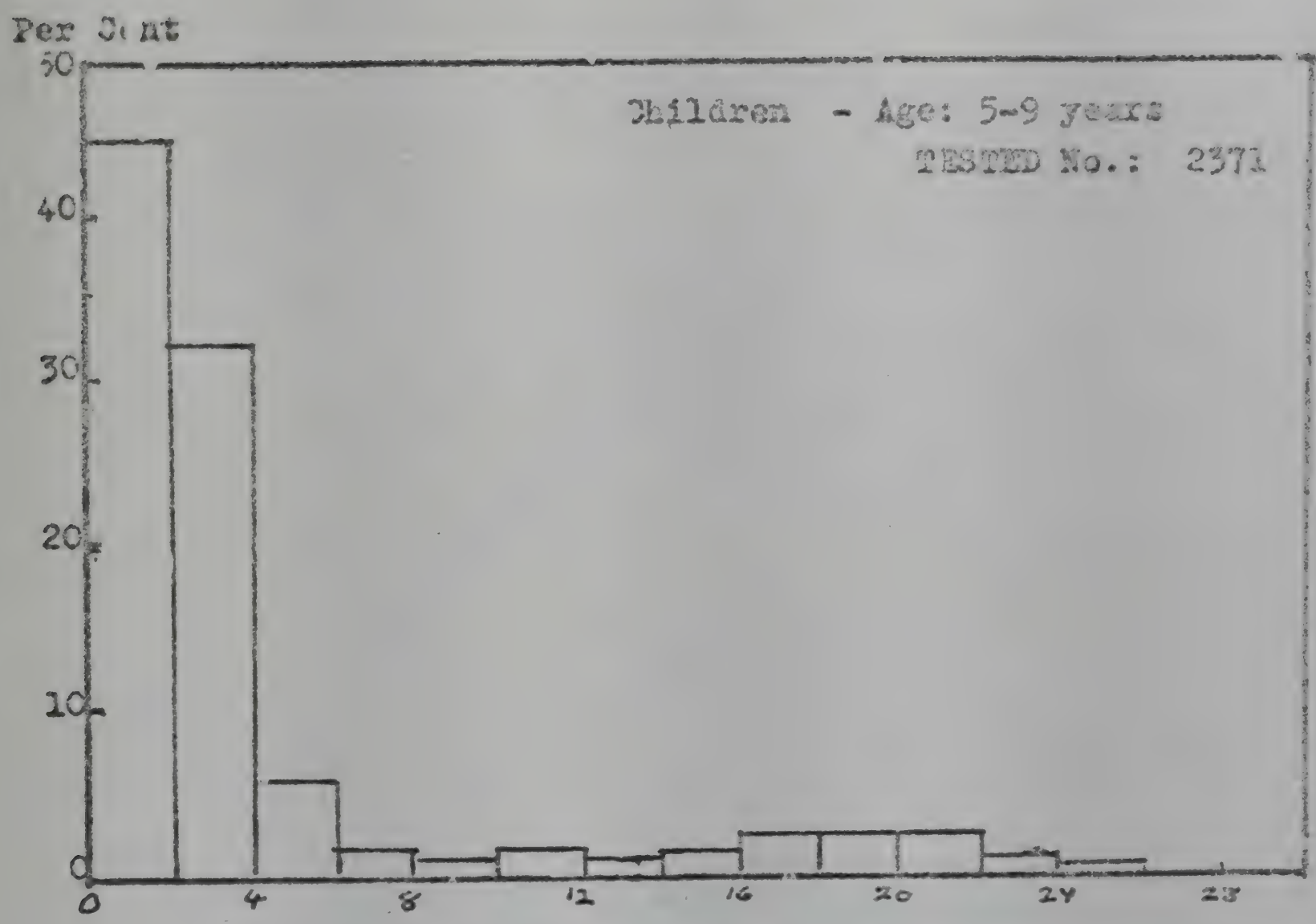
SURVEY 1965-68

SAMPLE SURVEY 1959

Graph 20


BOTH SEXES
Per 1000
10
5
0
0
5
10
Cases positive by Microscopy
1965 - 68
SURVEY III
10
5
0
0
5
10
Cases positive by Culture only
15
10
5
0
0
5
10
15 per 1000
Cases positive by Microscopy or Culture
SAMPLE SURVEY 1959

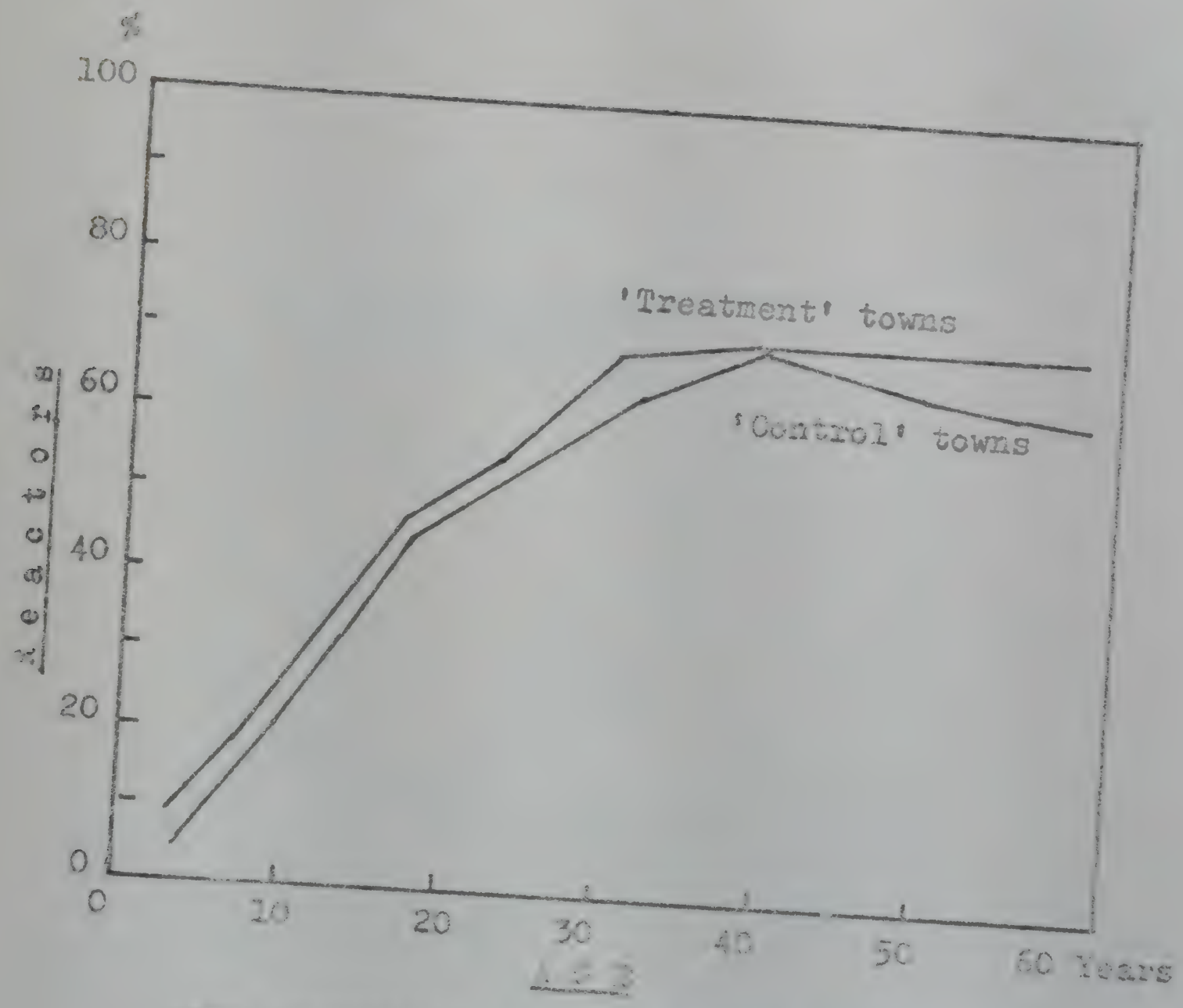
Graph 21.



Diameter of Indurations in Millimeters

1966-69 SAMPLE SURVEY

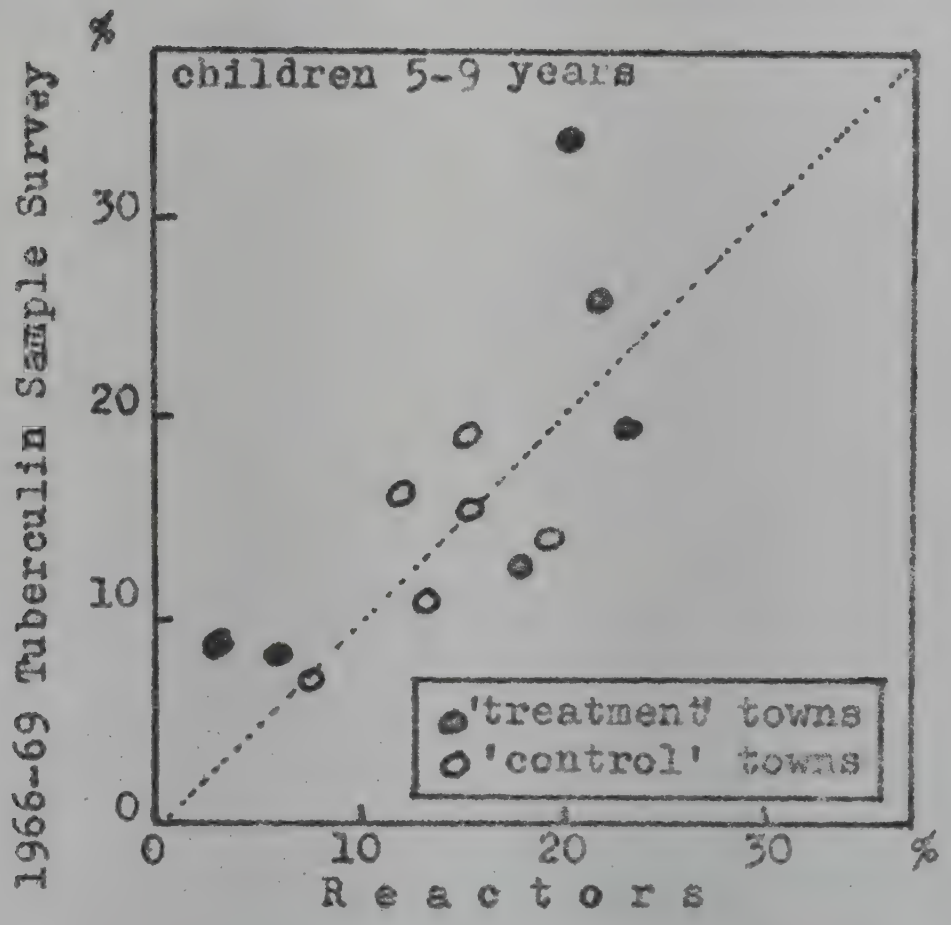
Graph 22.



Mean percentage of Reactors in 6 'treatment' and 6 'control' towns.

"Reactors" = persons with indurations of 8 mm or more to PPD-S 5 TU.

Graph 23.



1959 Tuberculin Sample Survey

Graph 24.

Table I

Efficacy of Microscopy, Cultures by H_2SO_4 and Cultures by NaOH in demonstrating TB in 650 sputum specimens.

(a)

Microscopy	Culture (H_2SO_4)	Culture (NaOH)	Specimens positive for TB No.
+	+	+	33
+	+	–	0
+	–	+	15
+	–	–	0
–	+	+	33
–	+	–	0
–	–	+	58
–	–	–	511
			650
+			48
	+		66
		+	139

(b)

Positive by Microscopy		Positive by Culture		
TB	No.	H_2SO_4 No.	NaOH No.	Gain by NaOH No.
+++	3	3	3	–
++	11	10	11	1
+	34	20	34	14
–		33	91	58
Total	48	66	139	73

Table II

1959 Sample Survey

Number of Blocks in Stratum I (20-40 house holds) and Stratum II (more than 40 households)

TOWNS	Stratum I		Stratum II		Total		
	Blocks		Blocks		Blocks		
	Total	Sample	Total	Sample	Total	Sample No.	Sample %
Kadiri	81	16	14	3	95	19	20.0
Rayachoti	90	18	6	1	96	19	19.8
Rajampet	81	17	11	2	92	19	20.6
Chintamani	100	20	7	2	113	22	19.5
*) Srinivaspur	41	11	3	1	44	12	27.3
Mulbagal	74	16	3	1	77	17	22.1
Tiruttani	53	15	6	1	59	16	27.1
*) Nagari	40	10	6	2	46	12	26.1
*) Puttur	41	13	9	2	50	15	30.0
Kalahasti	155	31	17	4	172	35	20.3
*) Palmaner	44	11	11	3	55	14	25.5
Punganur	57	11	19	4	76	15	19.7

*) Sample Fractions 25%, the remainders 20% .

Table III

1959 Sample Survey

Sample Fraction and No. of persons living in the Sample Blocks.

TOWNS	House holds in All Blocks No.	House holds in Sample Blocks No.	Sample Fraction %	Persons living in Sample Blocks No.
Kadiri	3714	658	17.7	2519
Rayachoti	2863	572	20.0	2116
Rajampet	2699	519	19.2	2158
Chintamani	3283	654	19.9	3436
Srinivasapur	1236	307	24.8	1695
Mulbagal	2064	425	20.6	2478
Tiruttani	2022	436	21.6	1730
Nagari	1457	366	25.1	1726
Puttur	1711	422	24.1	2137
Kalahasti	5116	1053	20.6	4116
Palmaner	1828	473	25.9	

Table IV

Comparison of town populations according to Census of India and the 1959 Sample Survey

TOWNS	Census 1951	Annual Growth Rate %	Estimated Population 1959	1959 Survey All Blocks No.	%
	(a)	(b)	(c)	(d)	(e)
Kadiri	20,354	1.79	23,458	14,218	60.6
Rayachoti	10,655	4.61	15,281	10,591	69.3
Rajampet	9.281	2.29	11,124	11,222	100.9
Chintamani	14,411	3.15	18,469	19,248	93.4
Srinivasapur	5,978	1.31	6,634	6,824	102.9
Mulbagal	9,025	2.87	11,318	12,034	106.3
Tiruttani	9,925	0.39	10,239	8,023	78.4
Nagari	6,567	2.01	7,700	6,871	89.2
Puttur	7,989	2.35	9,620	8,664	90.1
Kalahasti	17,921	3.97	24,470	22,422	91.6
Palmaner	6,884	3.66	9,178	8,019	87.4
Punganur	11,284	2.04	13,263	11,646	87.8

Table V

Prevalence of bacillary pulmonary tuberculosis in males and females per 1000 adults.

	Eligible persons	X-rayed*)		Selected for Bact.	Examined bacteriologically		Cases with TB in expectorate	
	No.	No.	%	No.	No.	%	No.	°/oo
Males								
Kadiri	736	674	91.6	104	89	85.6	8	13.9
Rayachoti	668	603	90.3	91	79	86.8	12	22.9
Rajampet	700	660	94.3	74	65	87.8	13	22.4
Chintamani	1067	968	90.7	76	63	82.9	2	2.5
Srinivasapur	500	469	93.8	54	46	85.2	4	10.0
Mulbagal	733	676	92.2	77	65	84.4	3	5.3
Tiruttani	534	476	89.1	77	70	90.9	7	16.2
Nagari	543	487	89.7	98	89	90.8	5	11.3
Puttur	678	631	93.1	106	100	94.3	8	13.4
Kalahasti	1524	1404	92.1	210	194	92.4	33	25.4
Palmaner	597	534	89.4	51	43	84.3	4	8.9
Punganur	651	590	90.6	62	53	85.5	2	4.0
Females								
Kadiri	715	640	89.5	60	57	95.0	3	4.9
Rayachoti	587	517	88.1	44	36	81.8	0	0.0
Rajampet	706	635	89.9	56	53	94.6	3	5.0
Chintamani	993	905	91.1	64	53	82.8	5	6.7
Srinivasapur	514	461	89.7	39	37	94.9	2	4.6
Mulbagal	690	625	90.6	54	43	79.6	1	2.0
Tiruttani	553	488	88.2	46	43	93.5	0	0.0
Nagari	519	466	89.8	46	45	97.8	3	6.6
Puttur	654	593	90.7	72	65	90.3	6	11.2
Kalahasti	1491	1389	93.2	132	129	97.7	13	9.6
Palmaner	598	553	92.5	34	31	91.2	1	2.0
Punganur	704	606	86.1	36	36	100.0	3	5.0

*) Films with technical errors are excluded.

Table VI

1959 Sample Survey

Readings by the Independent Assessor.

TOWNS	Persons X-rayed No.	Cases with radiological evidence of pulmonary pathology*)					
		A	B	C	D	E	Total
Kadiri	1349	13	7	47	30	4	101
Rayachoti	1154	8	8	52	40	4	112
Rajampet	1317	15	7	48	33	6	109
Chintamani	1878	22	8	67	31	14	142
Srinivasapur	931	6	3	29	19	6	63
Mulbagal	1310	22	4	33	27	8	94
Tiruttani	997	11	7	35	21	7	81
Nagari	974	15	4	46	23	11	99
Puttur	1242	11	8	50	38	8	115
Kalahasti	2806	35	16	153	100	23	327
Palamaner	1111	14	1	26	16	5	62
Punganur	1231	9	6	29	28	9	81

*) A = Probably non-tuberculous
B = Probably tuberculous but probably inactive
C = Probably tuberculous but possibly active
D = Probably tuberculous and probably active
E = Etiology very doubtful, or classification not possible.

Table VII

1959 Sample Survey

Prevalence of radiologically positive cases (Categories C and D) according to the Independent assessor.

TOWNS	Males			Females			Both Sexes
	X-rayed*) No.	C & D No.	C & D %	X-rayed*) No.	C & D No.	C & D %	C & D Cases %
Kadiri	671	51	7.6	637	26	4.1	5.9
Rayachoti	601	68	11.3	514	24	4.7	8.3
Rajampet	658	55	8.4	632	26	4.1	6.3
Chintamani	968	50	5.2	905	48	5.3	5.2
Srinivasapur	469	28	6.0	460	20	4.3	5.2
Mulbagal	676	38	5.6	626	22	3.5	4.6
Tiruttani	475	33	6.7	488	23	4.7	5.8
Nagari	486	49	10.1	465	20	4.3	7.3
Puttur	631	49	7.8	593	39	6.6	7.2
Kalahasti	1403	170	12.1	1389	83	6.0	9.1
Palamaner	534	25	4.7	553	17	3.1	3.9
Punganur	589	40	6.8	607	16	2.6	4.7

*) Films with technical errors are excluded.

Table VIII

1959 Sample Survey

Mantoux Tests with PPD-RT23 (1 T.U. + Tween 80) of children in age groups 5-9 y ears.

TOWNS	Schools	Student strength standards I & II	Children tested	Tests read	"BCG Scar" seen	Persons without "BCG Scar"	Reactors *)	
	No.			No.	No.	No.	No.	%
Kadiri	10	538	523	445	129	316	74	23.4
Rayachoti	8	673	385	338	7	331	51	15.4
Rajampet	8	660	328	273	56	217	45	20.7
Chintamani	8	1020	701	646	144	503	93	18.5
Srinivasapur	7	503	301	251	51	200	27	13.5
Mulbagal	8	644	438	361	92	269	20	7.4
Tiruttani	3	308	186	160	12	148	5	3.4
Nagari	4	390	236	205	19	186	29	15.6
Puttur	4	484	259	228	2	226	44	19.5
Kalahasti	16	1459	739	643	105	538	118	21.9
Palmaner	3	455	247	202	7	195	12	6.2
Punganur	5	720	344	300	6	207	25	12.1

*) Persons with reactions (indurations) measuring 6mm or more in transverse diameter.

Table IX

1959 Sample Survey

Indices of Tuberculosis Prevalence used at the randomization of the 12 Towns (both sexes).

TOWNS	Bacillary cases (adults)	Radiologically active cases	Tuberculin Reactors School children 5-9 Years
	°/oo	%	%
Kadiri	9.4	5.8	23.4
Rayachoti	12.6	8.3	15.4
Rajampet	13.6	6.2	20.7
Chintamani	4.5	5.2	18.5
Srinivasapur	7.2	5.2	13.5
Mulbagal	3.7	4.6	7.4
Tiruttani	7.9	5.7	3.4
Nagari	9.0	7.3	15.6
Puttur	12.3	7.1	19.5
Kalahasti	17.4	8.9	21.9
Palmaner	5.3	3.9	6.2
Punganur	4.6	4.7	12.1

Table X

Allocation of the 12 towns to 3 treatment groups (T1, T2 and C) according to the design of experiment.

Treatment Regimens	Towns	Prevalence of bacillary tuberculosis per 1000 adults	Comparisons
INH-PAS (T1)	Kalahasti	17.4	T1-T2 = $2.03 \pm 4.44^{o}/_{oo}$ (Not significant)
	Kadiri	9.4	
	Palmaner	5.3	
	Mean:	10.70	
INH (T2)	Rajampet	13.6	
	Tiruttani	7.9	
	Chintamani	4.5	
	Mean:	8.67	
All 6 towns	Mean:	9.68	(T1+T2) - C = $1.45 \pm 2.5^{o}/_{oo}$ (Not significant)
Nil (C)	Rayachoti	12.6	
	Puttur	12.3	
	Nagari	9.0	
	Srinivasapur	7.2	
	Mulbagal	3.7	
	Punganur	4.6	
	Mean:	8.23	

Table XI

Number of bacillary cases diagnosed and treated.

Towns	Number diagnosed	Cases with observation period < 1 year	Number died or moved out	Number available for treatment	Treated No.
Kadiri	417	21	18	378	351
Palmaner	100	5	4	91	86
Kalahasti	640	86	56	498	403
Rajampet	299	7	20	272	240
Chintamani	164	2	11	151	117
Tiruttani	161	55	14	92	69
Total	1781	176	123	1482	1266

Table XII

Distribution of bacillary cases according to radiological extent of disease.

Towns	Cases No.	Trivial & slight %	Limited %	Moderate %	Extensive & gross %
(a) Cases initially positive by Microscopy (M+)					
Kadiri	215	7.0	15.4	35.8	41.8
Palmaner	43	13.9	23.3	34.9	27.9
Kalahasti	260	6.2	18.1	35.0	40.8
Rajampet	148	2.1	15.5	37.8	44.6
Chintamani	63	6.4	19.0	49.2	25.4
Tiruttani	82	7.3	14.6	41.5	36.6
Mean:		7.2	17.7	39.0	36.2
(b) Cases initially positive by Culture only (C+)					
Kadiri	187	29.9	32.1	28.3	9.6
Palmaner	52	17.3	32.7	40.4	9.6
Kalahasti	335	29.8	27.2	28.1	14.9
Rajampet	134	20.9	29.1	29.9	20.1
Chintamani	92	29.3	26.1	34.8	9.8
Tiruttani	71	32.4	25.3	26.8	15.5
Mean:		26.6	28.8	31.4	13.3

Table XIII

Distribution of bacillary cases according to radiological evidence of cavities.

Towns	Cases (=100%)	Cavities			
		Nil	Slight	Moderate	Extensive
	No.	%	%	%	%
(i) Cases initially positive by Microscopy					
Kadiri	215	15.8	27.9	38.1	18.1
Palmaner	43	18.6	32.6	32.6	16.3
Kalahasti	260	15.8	28.8	27.7	27.7
Rajampet	148	9.5	26.3	33.8	30.4
Chintamani	63	15.9	30.1	28.6	25.4
Tiruttani	82	23.2	30.5	23.2	23.2
Mean:		16.5	29.4	30.7	23.5
(ii) Cases initially positive by Culture only					
Kadiri	187	58.8	27.8	9.6	3.7
Palmaner	52	55.8	38.5	1.9	3.8
Kalahasti	335	58.5	25.4	10.7	5.4
Rajampet	134	47.8	29.9	16.4	6.0
Chintamani	92	48.9	39.1	5.4	6.5
Tiruttani	71	50.7	35.2	11.3	2.8
Mean:		53.4	32.7	9.2	4.7

Table XIV

Comparison of "Isoniazid-PAS" towns with "INH" towns with regard to Extent of disease and Cavitation.

Group	Trivial & Slight	Limited	Moderate	Extensive & Gross
A. Extent of Disease	%	%	%	%
(i) M+				
INH-PAS	9.0	18.9	35.2	38.8
INH	5.3	16.4	42.8	35.5
(ii) C+				
INH-PAS	25.6	30.7	32.3	11.3
INH	27.5	26.8	30.5	15.1
B. Cavities	Nil	Slight	Moderate	Extensive
(i) M+	%	%	%	%
INH-PAS	16.7	29.8	32.8	20.7
INH	16.2	29.0	28.5	26.3
(ii) C+				

Table XV

Percentage of patients accepting domiciliary treatment.

TOWNS	Males			Females			Both Sexes		
	Cases No.	Treated No.	%	Cases No.	Treated No.	%	Cases No.	Treated No.	%
(i) Cases initially positive by Microscopy (M+)									
Kadiri	135	130	96.3	64	62	96.9	199	192	96.5
Palmaner	29	27	93.1	13	13	100.0	42	40	95.2
Kalahasti	157	143	91.1	50	43	86.0	207	186	89.9
Rajampet	103	97	94.2	37	34	91.9	140	131	93.6
Chintamani	33	27	81.8	32	28	87.5	65	55	84.6
Tiruttani	37	31	83.8	11	9	81.8	48	40	83.3
Means:			90.1			90.7			90.5
(ii) Cases initially positive by Culture only (C+)									
Kadiri	128	111	86.7	51	48	94.1	179	159	88.8
Palmaner	30	29	96.7	19	17	89.5	49	46	93.9
Kalahasti	218	161	73.9	73	56	76.7	291	217	74.6
Rajampet	104	83	79.8	28	26	92.9	132	109	82.6
Chintamani	52	38	73.1	34	24	70.6	86	62	72.1
Tiruttani	34	24	70.6	10	4	40.0	44	28	63.6
Means:			80.1			77.3			79.3
(iii) All positive cases (M+ & C+)									
Kadiri	263	241	91.6	115	110	95.7	378	351	92.9
Palmaner	59	56	94.9	32	30	93.8	91	86	94.5
Kalahasti	375	304	81.1	123	99	80.5	498	403	80.9
Rajampet	207	180	87.0	65	60	92.3	272	240	88.2
Chintamani	85	65	76.5	66	52	78.8	151	117	77.5
Tiruttani	71	55	77.5	21	13	61.9	92	68	73.9
Means:			84.8			83.8			84.7

Table XVI

Percentage of patients under treatment every 3 months.

(Both Sexes)

TOWNS	Cases No.	Months				
		0	3	6	9	12
(i) Cases initially positive by Microscopy (M+)						
Kadiri	199	96.5	91.6	86.4	81.0	78.0
Palmaner	42	95.2	90.2	90.0	82.1	73.7
Kalahasti	207	89.9	81.2	74.2	68.1	61.8
Rajampet	140	93.6	81.1	74.6	71.3	62.1
Chintamani	65	84.6	80.0	71.7	67.8	55.2
Tiruttani	48	83.3	79.2	68.9	65.1	46.3
Means:		90.5	83.9	77.6	72.6	62.9
(ii) Cases initially positive by Culture only (C+)						
Kadiri	179	88.8	79.2	70.7	64.5	57.1
Palmaner	49	93.9	83.0	80.4	73.9	67.4
Kalahasti	291	74.6	63.4	54.8	47.1	40.2
Rajampet	132	82.6	71.2	62.5	52.8	44.8
Chintamani	86	72.1	62.8	50.0	49.4	47.0
Tiruttani	44	63.6	63.6	54.5	50.0	41.9
Means:		79.3	70.5	62.2	56.3	49.7
(iii) All positives (M+ & C+)						
Kadiri	378	92.9	85.6	79.1	73.5	67.7
Palmaner	91	94.5	86.4	84.9	80.0	70.2
Kalahasti	498	80.9	70.7	62.6	55.6	48.9
Rajampet	272	88.2	76.1	68.5	61.9	53.1
Chintamani	151	77.5	69.9	59.0	57.0	50.4
Tiruttani	92	73.9	71.7	61.8	57.5	44.1
Means:		84.7	76.7	69.3	64.3	55.7

Table XVII

Co-operation of patients under domiciliary treatment

I t e m s	Patients treated %[1)]	Defaulter rate per month %
A. TOWNS:		
Kadiri	81.3	1.93
Palmaner	82.4	2.10
Kalahasti	66.8	2.32
Rajampet	71.3	2.65
Chintamani	63.7	2.33
Tiruttami	58.8	2.46
Means:	71.7	2.30
B. COMPARISONS:		
(i) Sex:		
Males	70.6	2.34
Females	70.8	2.26
Differences:	-0.2	0.08
(ii) Initial Sputum Examinations:		
By microscopy	78.2	2.29
By culture only	63.2	2.31
Differences:	15.0**	-0.02
(iii) Drug Regimens:		
INH-PAS	76.8	2.12
INH	64.6	2.48
Differences:	12.2**	-0.37**
(iv) Interactions:		
Sex x diagnosis	5.3*	
Sex x regimens	3.8**	

1) Mean of 12 months observation.

Table XVIII

Treatment Results at the end of the year

Both Sexes

Towns	Cases No.	Died %	TB+ %	TB - %
(a) Cases initially positive by microscopy (M+)				
Kadiri	192	10.5	33.1	56.4
Palmaner	40	5.1	21.7	73.2
Kalahasti	186	13.8	44.9	41.3
Rajampet	131	18.9	49.2	31.9
Chintamani	55	5.9	51.2	43.0
Tiruttani	40	18.9	44.7	36.3
Means:		12.2	40.9	47.0
(b) Cases initially positive by culture only (C+)				
Kadiri	159	3.9	31.1	65.0
Palmaner	46	6.7	18.2	75.1
Kalahasti	217	6.7	28.5	64.9
Rajampet	109	7.6	41.6	50.8
Chintamani	62	5.1	42.8	52.1
Tiruttani	29	6.9	31.0	62.1
Means:		6.2	32.2	61.7
(c) All Cases (M+ & C+)				
Kadiri	351	7.5	32.2	60.3
Palmaner	86	6.2	19.8	74.1
Kalahasti	403	10.0	36.2	53.8
Rajampet	240	13.7	45.7	40.6
Chintamani	117	5.5	46.8	47.8
Tiruttani	69	13.6	38.6	47.8
Means:		9.4	36.6	54.1

Table XIX

Treatment Results at the End of One Year

Towns	MALES				FEMALES			
	Cases No.	Died %	TB+ %	TB– %	Cases No.	Died %	TB+ %	TB– %
(a) Cases positive initially by microscopy (M+)								
Kadiri	130	12.2	35.6	52.2	62	6.9	28.1	65.0
Palmaner	27	7.6	20.1	72.2	13	0.0	25.0	75.0
Kalahasti	143	15.1	43.6	41.3	43	9.5	49.1	41.4
Rajampet	97	18.9	48.7	32.4	34	18.8	50.8	30.5
Chintamani	27	4.0	60.0	36.0	28	7.7	42.0	50.3
Tiruttani	31	17.9	44.8	37.3	9	22.2	44.4	33.3
Means:		12.6	42.1	45.2		10.9	39.9	49.3
(b) Cases initially positive by culture only (C+)								
Kadiri	111	3.7	34.7	61.6	48	4.3	22.8	72.9
Palmaner	29	3.4	17.2	79.3	17	12.5	20.2	67.3
Kalahasti	161	7.1	28.6	64.3	56	5.5	28.2	66.4
Rajampet	83	7.5	43.5	49.0	26	8.0	36.0	56.0
Chintamani	38	5.4	50.3	44.3	24	4.5	30.1	65.3
Tiruttani	25	4.0	36.0	60.0	4	25.0	0.0	75.0
Means:		5.2	35.1	59.8		10.0	22.9	67.1
(c) All cases (M+ & C+)								
Kadiri	241	8.2	35.2	56.6	110	5.8	25.8	68.4
Palmaner	56	5.5	18.5	76.0	30	6.9	22.3	70.8
Kalahasti	304	10.9	35.8	53.3	99	7.2	37.3	55.4
Rajampet	180	13.5	46.4	40.1	60	14.0	43.9	42.1
Chintamani	65	4.8	54.4	40.8	52	6.3	36.6	57.2
Tiruttani	56	11.3	40.5	48.2	13	23.1	30.8	46.2
Means:		9.0	38.5	52.5		10.6	32.8	56.7

Table XX

Treatment Results at the End of One Year

A. Cases with Isoniazid-sensitive strains initially.

Towns	Males				Females			
	Cases No.	Died %	TB+ %	TB- %	Cases No.	Died %	TB+ %	TB- %
(a) M+								
Kadiri	99	11.7	34.0	54.3	45	7.0	28.6	64.4
Palmaner	22	9.5	19.0	71.4	9	0.0	22.2	77.8
Kalahasti	99	13.4	36.0	50.6	20	10.0	37.1	52.9
Rajampet	67	15.9	46.2	37.9	25	12.0	48.4	39.6
Chintamani	17	0.0	56.3	43.8	14	0.0	27.3	72.7
Tiruttani	22	10.0	47.6	42.4	5	(40.0)	(20.0)	(40.0)
Means:		10.1	39.9	50.1		11.5	30.6	57.9
(b) C+								
Kadiri	101	3.1	36.4	60.5	39	5.3	16.7	78.0
Palmaner	29	3.4	17.2	79.3	13	7.7	16.8	75.5
Kalahasti	137	6.0	29.7	64.3	40	2.5	19.5	78.0
Rajampet	75	6.9	41.2	51.9	21	4.8	33.3	61.9
Chintamani	27	7.7	52.7	39.6	18	5.6	25.2	69.3
Tiruttani	22	4.5	36.4	59.1	4	(25.0)	(0.0)	(75.0)
Means:		5.3	35.6	59.1		8.5	18.6	73.0
(c) All Cases (M+ & C+)								
Kadiri	200	7.3	35.2	57.5	84	6.2	23.1	70.7
Palmaner	51	6.0	18.0	76.0	22	4.5	19.1	76.4
Kalahasti	236	9.1	32.4	58.5	60	5.0	25.6	69.4
Rajampet	142	11.1	43.7	45.2	46	8.7	41.1	50.2
Chintamani	44	4.8	54.1	41.2	32	3.2	26.1	70.7
Tiruttani	44	7.1	41.5	51.3	9	(33.3)	(11.1)	(55.6)
Means:		7.6	37.5	55.0		10.2	24.4	65.5

Note: M+ = Cases positive by microscopy
C+ = Cases positive by culture only

Contd....

Table XX Contd.....

Treatment Results at the End of One Year

B. Cases with Isoniazid-resistant strains initially.

Towns	Males				Females			
	Cases No.	Died %	TB+ %	TB- %	Cases No.	Died %	TB+ %	TB- %
(a) M+								
Kadiri	17	25.0	50.0	25.0	10	0.0	25.0	75.0
Palmaner	1	(0.0)	(100.0)	(0.0)	2	(0.0)	(0.0)	(100.0)
Kalahasti	32	19.4	70.1	10.5	20	10.5	67.1	22.4
Rajampet	24	33.3	61.5	5.1	7	60.0	40.0	0.0
Chintamani	8	0.0	85.7	14.3	8	28.6	57.1	14.3
Tiruttani	4	(50.0)	(25.0)	(25.0)	3	(0.0)	(100.0)	(0.0)
Means:		19.4	66.8	13.7		24.8	47.3	27.9
(b) C+								
Kadiri	7	14.3	28.6	57.1	8	0.0	57.1	42.9
Palmaner	0	-	-	-	4	33.3	33.3	33.3
Kalahasti	22	14.3	22.9	62.9	14	14.3	46.8	39.0
Rajampet	8	12.5	62.5	25.0	4	25.0	50.0	25.0
Chintamani	10	0.0	50.0	50.0	6	0.0	50.0	50.0
Tiruttani	3	(0.0)	(33.3)	66.7	0	0.0	0.0	0.0
Means:		10.3	41.0	48.7		9.8	51.0	39.2
(c) All cases (M+ & C+)								
Kadiri	24	21.7	43.5	34.8	18	0.0	40.0	60.0
Palmaner	1	(0.0)	(100.0)	(0.0)	6	20.0	26.7	53.3
Kalahasti	54	17.3	52.2	30.5	34	3.0	64.6	32.3
Rajampet	32	27.6	61.6	10.9	11	44.4	44.4	11.1
Chintamani	18	0.0	64.7	35.3	14	18.2	54.5	27.3
Tiruttani	7	(28.6)	(28.6)	(42.9)	3	(0.0)	(100.0)	(0.0)
Means:		16.7	55.5	27.9		16.4	50.9	32.7

Note: M+ = Cases positive by microscopy.
C+ = Cases positive by culture only.

Table XXI

Treatment results at the end of one year

A. Cases with Isoniazid Sensitive strains initially

Both Sexes

Towns	Cases No.	Died %	TB+ S %	TB+ R %	TB- %
(a) M+					
Kadiri	144	10.2	14.0	18.2	57.6
Palmaner	31	6.7	3.3	16.7	73.3
Kalahasti	119	12.8	20.1	16.1	51.0
Rajampet	92	14.8	14.8	32.0	38.4
Chintamani	31	0.0	14.8	29.6	55.6
Tiruttani	27	16.0	8.4	33.6	42.0
Means:		10.1	12.6	24.4	53.0
(b) C +					
Kadiri	140	3.7	23.5	7.3	65.5
Palmaner	42	4.8	17.1	0.0	78.1
Kalahasti	177	5.2	19.9	7.5	67.4
Rajampet	96	6.5	23.1	16.2	54.3
Chintamani	45	6.8	28.5	12.9	51.8
Tiruttani	26	7.7	27.0	3.8	61.5
Means:		5.8	23.4	8.0	63.1
(c) all cases (M+ & C+)					
Kadiri	284	7.0	18.8	12.7	61.5
Palmaner	73	5.6	11.3	7.0	76.1
Kalahasti	296	8.3	20.0	11.0	60.8
Rajampet	188	10.5	19.1	23.9	46.5
Chintamani	76	4.1	22.8	19.8	53.3
Tiruttani	53	11.8	18.1	18.1	52.1
Means:		7.9	18.4	15.4	58.4

Table XXI contd....

Treatment results at the end of one year

B. Cases with Isoniazid Resistant Strains initially.

Both Sexes

Towns	Cases	Died	TB+		TB-
			S	R	
	No.	%	%	%	%
(a) M+					
Kadiri	27	16.7	4.2	37.5	41.7
Palmaner	3	0.0	0.0	50.0	50.0
Kalahasti	52	16.0	4.4	64.5	15.1
Rajampet	31	38.5	0.0	57.4	4.1
Chintamani	16	14.3	0.0	71.4	14.3
Tiruttani	7	50.0	0.0	40.0	10.0
Means:		22.6	1.4	53.5	22.5
(b) C+					
Kadiri	15	13.3	13.3	26.7	46.7
Palmaner	4	33.3	0.0	33.3	33.3
Kalahasti	36	14.3	3.7	29.3	52.7
Rajampet	12	16.7	0.0	58.3	25.0
Chintamani	16	0.0	0.0	50.0	50.0
Tiruttani	3	0.0	0.0	33.3	66.7
Means:		12.9	2.8	38.5	45.7
(c) all cases (M+ & C+)					
Kadiri	42	15.4	7.7	33.3	43.6
Palmaner	7	16.7	0.0	41.6	41.6
Kalahasti	88	15.3	4.1	50.6	30.0
Rajampet	43	31.6	0.0	57.4	11.0
Chintamani	32	7.1	0.0	60.7	32.2
Tiruttani	10	20.0	0.0	50.0	30.0
Means		17.7	2.0	48.9	31.4

Table XXII

Comparison of treatment results in INH-PAS and INH Towns (Ref.Tables XVIII & XIX).

Sex	Initial sputum examination	Treatment Group	Result at one year		
			Died	TB+	TB-
			%	%	%
Both Sexes	M+	INH-PAS	9.8	33.2	57.0
		INH	14.6	48.4	37.1
		Differences	-4.8	-15.1**	19.9**
	C+	INH-PAS	5.8	25.9	68.3
		INH	6.5	38.5	55.0
		Differences:	-0.8	-12.5**	13.3**
	All (M+ & C+)	INH-PAS	7.9	29.4	62.7
		INH	10.9	43.7	45.4
		Differences	-3.0	-14.3**	17.3**
Males	M+	INH-PAS	11.6	33.1	55.2
		INH	13.6	51.2	35.2
		Differences:	-2.0	-18.1**	20.0**
	C+	INH-PAS	4.7	26.8	68.4
		INH	5.6	43.3	51.1
		Differences:	-0.9	-16.4**	17.3**
	All (M+ & C+)	INH-PAS	8.2	29.8	62.0
		INH	9.9	47.1	43.0
		Differences:	-1.7	-17.3**	18.9**
Females	M+	INH-PAS	5.5	34.1	60.5
		INH	16.2	45.7	38.0
		Differences:	-10.8	-11.6	22.4
	C+	INH-PAS	7.4	23.7	68.9
		INH	12.5	22.0	65.4
		Differences:	-5.1	1.7	3.5
	All (M+ & C+)	INH-PAS	6.6	28.5	64.9
		INH	14.5	37.1	48.5
		Differences:	-7.8	-8.6	16.4*

Table XXIII

Comparison of Isoniazid sensitivity results at the end of one year of treatment in INH-PAS and INH towns (Ref. Table XXI)

(Both Sexes)

Initial sputum examination	Treatment Group	Treatment Result at one year			
			TB+		
		Died	S	R	TB-
A. Cases with initially Isoniazid sensitive bacilli					
M+	INH-PAS	9.9	12.5	17.0	60.6
	INH	10.3	12.7	31.7	45.3
	Differences	-0.4	-0-2	-14.7**	15.3**
C+	INH-PAS	4.6	20.2	4.9	70.3
	INH	7.0	26.2	11.0	55.9
	Differences	-2.4	-6.0	-6.0**	14.5**
All (M+ & C+)	INH-PAS	7.0	16.7	10.2	66.1
	INH	8.8	20.0	20.4	50.6
	Differences	-1.8	-3.3	-10.4**	15.5**
B. Cases with initially Isoniazid resistant bacilli					
M+	INH-PAS	10.9	2.9	50.7	35.6
	INH	34.3	0.0	56.3	9.5
	Differences	-23.4*	2.9	5.6	26.1*
C+	INH-PAS	20.3	5.7	29.8	44.2
	INH	5.6	0.0	47.2	47.2
	Differences	14.7	5.7	-17.4	-3.0
All (M+ & C+)	INH-PAS	15.8	3.9	41.8	38.4
	INH	19.6	0.0	56.0	24.4
	Differences	-3.8	3.9	-14.2	14.0

Table XXIV

Five Years' Follow-up

Follow-up Study of all cases from the 6 'Treatment' Towns whether treated or untreated.

Number: 1449

Year of Observation	Died	Sputum	
		Positive (TB+)	Negative (TB-)
	%	%	%
1	14.6	35.8	49.6
2	23.7	32.1	44.2
3	31.1	24.9	44.0
4	36.2	19.9	43.9
5	40.4	18.2	41.4

Table XXV

Five Years' Follow-up

Follow-up Study of 1154 Treated Cases according to initial radiological extent of disease*).

Years of Observation	"Trivial" "Slight" (194)			"Limited" (235)			"Moderate" (406)			"Extensive" "Gross" (319)		
	Died	TB+	TB-	Died	TB+	TB-	Died	TB+	TB-	Died	TB+	TB-
	%	%	%	%	%	%	%	%	%	%	%	%
1	4.8	22.3	72.9	5.2	31.6	63.2	5.9	41.9	52.2	20.4	45.9	33.7
2	6.5	22.8	70.7	11.1	31.3	57.6	13.5	38.3	48.2	36.6	35.6	27.8
3	11.9	20.9	67.2	16.0	27.8	56.2	20.3	30.2	49.5	47.2	26.8	26.0
4	15.5	16.4	68.1	21.4	21.1	57.5	25.3	25.8	48.9	54.8	18.5	26.7
5	19.1	11.6	69.3	24.5	21.7	53.8	31.9	24.9	44.1	58.2	16.7	25.1

Table XXVI

Five Years' Follow-up

Follow-up results of 1086 treated cases according to initial bacillary sensitivity to Isoniazid.

Years	INH-Sensitive (887)			INH-Resistant (199)		
	Died %	TB+ %	TB- %	Died %	TB+ %	TB- %
1	8.0	34.1	57.9	17.6	55.4	27.1
2	15.8	31.8	52.4	29.9	42.4	27.7
3	22.5	27.6	49.9	37.7	25.8	36.5
4	27.4	22.1	50.5	43.7	18.8	37.5
5	32.0	21.7	46.3	44.4	14.2	41.4

Table XXVII

Five Years' Follow-up.

Results of 911 cases according to their bacteriological status one year after starting domiciliary treatment.

Year of Observation	Sputum-negative (532)			Sputum-positive (379)		
	Died %	TB+ %	TB- %	Died %	TB+ %	TB- %
2	3.4	17.2	79.4	18.4	65.6	16.0
3	6.9	18.6	74.5	31.9	44.9	23.2
4	10.9	13.4	75.7	40.2	38.1	21.7
5	13.3	16.6	69.6	47.8	28.3	23.9
6	18.0	15.9	66.1	56.0	20.2	23.8

Table XXVIII

Mortality

Average Annual Death Rates per 1000 due to All Causes

Age Group	Kadiri	Palmaner	Kalahasti	Rajampet	Chintamani	Tiruttani
Males						
0-	7.4	4.8	4.6	4.6	7.3	6.6
15-	2.7	4.4	4.8	5.7	3.2	4.7
25-	3.7	4.5	9.1	9.2	4.1	5.3
35-	8.3	5.7	16.5	13.4	6.4	16.7
45-	22.5	14.9	28.8	27.0	12.2	22.0
55+	44.3	56.5	67.3	63.5	49.8	61.7
All Males	9.4	9.1	13.1	13.0	9.0	12.8
Females						
0-	9.2	6.0	5.8	4.9	5.7	6.4
15-	3.9	4.8	5.7	8.8	4.2	4.4
25-	4.9	3.5	6.2	6.6	2.9	5.1
35-	6.0	4.0	8.0	8.0	4.9	10.2
45-	12.3	8.6	15.4	19.0	12.9	16.2
55+	37.2	42.1	51.9	55.4	42.9	55.0
All Females	9.2	7.8	10.4	11.6	7.6	10.3
All	9.3	8.4	11.8	12.3	8.3	11.6

Table XXIX

Mortality

Annual Death Rates per 100,000 from Tuberculosis*)

Age Group	Kadiri	Palmaner	Kalahasti	Rajampet	Chintamani	Tiruttani
Males						
15-24	38	0	81	91	0	62
25-34	61	43	238	175	51	91
35-44	194	52	342	342	18	235
45-54	397	109	604	599	92	267
55+	452	140	851	783	56	537
All males	95	31	208	204	21	129
Females						
15-24	12	38	35	80	52	20
25-34	63	19	88	169	111	82
35-44	72	0	132	138	49	0
45-54	61	112	112	204	23	130
55+	102	47	51	210	62	103
All females	31	22	54	97	38	39

Table XXX

Mortality

Deaths among cases of Tuberculosis as Percentage of deaths due to All causes.

Age Group	Kadiri	Palmaner	Kalahasti	Rajampet	Chintamani	Tiruttani
Males	%	%	%	%	%	%
15–24	14.3	0.0	16.9	16.1	0.0	13.0
25–34	16.7	9.5	26.1	19.1	12.5	17.2
35–44	23.4	9.1	20.7	25.5	2.9	14.1
45–54	17.6	7.3	21.0	22.2	7.5	16.7
55+	10.2	2.5	12.6	12.3	1.1	8.7
All males	10.0	3.4	15.8	15.7	2.4	10.1
Females						
15–24	3.0	8.0	6.1	9.1	12.2	4.5
25–34	12.8	5.6	14.1	25.7	38.5	16.1
35–44	12.0	0.0	16.5	17.2	10.0	0.0
45–54	5.0	13.0	7.3	10.7	1.8	8.0
55+	2.8	1.1	1.0	3.8	1.5	1.9
All females	3.4	2.8	5.1	8.3	5.0	3.8
Both Sexes	6.8	3.1	11.1	12.3	3.6	7.3

Table XXXI

Mortality

Average death rates per 1000 in the 6 'Treatment' Towns

Age	Deaths from all causes		Deaths from Tuberculosis *)	
	Per 1000	95% fiducial limits	Per 1000	95% fiducial limits
A. Males				
0–	5.9	4.5 – 7.3	..	;; ..
15–	4.3	3.1 – 5.4	0.45	0.04 – 0.89
25–	6.0	3.4 – 8.6	1.10	0.27 – 1.93
35–	11.2	5.9 – 16.4	1.97	0.51 – 3.43
45–	21.2	14.4 – 28.1	3.61	1.25 – 5.97
55+	57.2	48.0 – 66.4	4.70	1.29 – 8.11
15–55+	14.17	10.34 – 18.00	1.15	0.29 – 2.00
all	11.1	8.9 – 13.3		
B. Females				
0–	6.3	4.8 – 7.9	..	.. ..
15–	5.3	3.4 – 7.2	0.40	0.14 – 0.65
25–	4.9	3.3 – 6.4	0.89	0.36 – 1.41
35–	6.9	4.4 – 9.3	0.65	0.01 – 1.29
45–	14.1	10.3 – 17.9	1.07	0.42 – 1.72
55+	47.4	39.4 – 55.5	0.96	0.32 – 1.60
15–55+	11.32	8.57 – 14.07	0.47	0.18 – 0.75
all	9.5	7.8 – 11.1		
Both Sexes				

Table XXXII

Average distribution of categories A,B & C*) 1960-68

Towns	Cases per 1000 adults per year(100%)	Cat. A %	Cat.B %	Cat. C %
Kadiri	8.7	40.2	16.1	43.7
Palmaner	3.4	50.0	14.7	35.3
Kalahasti	8.9	43.8	20.2	37.1
Rajampet	9.9	39.4	20.2	40.4
Chintamani	3.8	31.6	18.4	50.0
Tiruttani	4.6	50.0	15.2	34.8
Means		42.5	17.5	40.2

*) Initial bacteriological diagnosis done:-

(i) the same year - Category A.
(ii) the previous calender year - Category B.
(iii) earlier than the previous calender year - Category C.

Table XXXIII

Mean annual rates of proved sputum positive cases (per 1000 adults) according to sex showing percentage distributions of Categories A("NEW") and B+C("OLD")

Towns	Males *) A		B+C		Females *) A		B+C	
		%		%				%
Kadiri	2.22	37.0	3.78	63.0	1.12	48.3	1.20	51.7
Palmaner	0.49	47.8	1.08	52.2	0.54	54.5	0.45	45.5
Kalahasti	2.89	41.6	4.06	58.4	1.00	50.0	1.00	50.0
Rajampet	2.93	38.7	4.65	61.3	0.77	42.8	1.03	57.2
Chintamani	0.76	32.2	1.60	67.8	0.47	34.6	0.89	65.4
Tiruttani	1.42	41.4	2.01	58.6	0.62	57.9	0.45	42.1
Mean		39.8		60.2		48.0		52.0

*) Totals. of Males/Females = 100%

Table XXXIV

'Pool of Infectious Cases'

Bacillary cases per 1000 adults in each of the six treatment towns according to the Categories A ("NEW") and B+C ("OLD").

Year	Kadiri	Palmaner	Kalahasti	Rajampet	Chintamani	Tiruttani	MEAN
"NEW" CASES (A)							
1961	1.9	3.3	8.1	2.9	1.2	0.8	3.03
62	6.3	0.9	3.0	5.8	1.1	1.3	3.07
63	2.0	3.0	2.6	4.8	2.1	5.1	3.27
64	3.3	2.4	12.7	2.7	1.5	1.8	4.07
65	2.1	0.9	2.9	2.0	0.3	0.4	1.43
66	7.5	0.4	0.8	7.5	0.4	0.4	2.83
67	1.5	0.3	0.6	3.6	2.8	2.6	1.90
68	1.5	3.7	4.7	0.8	0.3	4.0	2.50
MEAN:	3.24	1.86	4.43	3.76	1.21	2.05	2.76
"OLD" CASES (B+C)							
1961	4.1	-	0.8	4.3	1.9	3.3	2.88
62	4.0	0.5	4.0	4.1	2.0	1.9	2.75
63	4.8	1.0	3.9	6.8	2.3	2.1	3.48
64	4.6	2.4	3.7	8.1	3.3	3.6	4.28
65	4.6	2.7	9.4	5.6	3.4	3.7	4.90
66	5.5	2.0	5.3	4.4	2.0	1.7	3.48
67	5.9	1.5	5.5	7.6	2.0	1.6	4.02
68	5.6	1.5	3.6	5.4	2.8	1.9	3.47
MEAN:	4.89	1.66	4.52	5.79	2.46	2.48	3.65

Table XXXV

'Pool of Infectious Cases'

Mean of bacillary cases (per 1000 adults) of observations in the 6 'Treatment' Towns according to Categories A ("New") and B+C ("Old") and the method of demonstrating the bacilli.[a)]

All Towns - both sexes

Year	"NEW" (A)			"OLD" (B+C)			Total		
	M+	C+	ALL	M+	C+	ALL	M+	C+	All
	°/oo	°/oo	°/oo	°/oo	°/oo	°/oo	°/oo	°/oo	°/oo
1960	3.13	1.50	4.63	0.33	0.02	0.35	3.46	1.52	4.98
61	1.79	1.25	3.04	1.68	0.70	2.38	3.47	1.95	5.42
62	1.76	1.30	3.06	2.06	0.69	2.75	3.82	1.99	5.81
63	1.73	1.56	3.29	2.40	1.14	3.54	4.13	2.70	6.83
64	1.51	2.55	4.06	2.40	1.86	4.26	3.91	4.41	8.32
65	0.64	0.78	1.42	2.42	2.49	4.91	3.06	3.27	6.33
66	1.36	1.49	2.85	1.97	1.50	3.47	3.33	2.99	6.32
67	1.05	0.84	1.89	2.36	1.66	4.02	3.41	2.50	5.91
68	1.58	0.93	2.51	2.38	1.08	3.46	3.96	2.01	5.97
b	-0.17*	-0.02	-0.24	0.17*	0.17	0.34*	0.00	-0.02	0.10
t_7	2.53	-	2.29	2.45	2.13	2.57	-	-	-

Note: *) $P < 0.05$; b = regression coefficient

a) M+ : Sputum positive by microscopy; C+ : Sputum positive only by culture.

Table XXXVI

'Pool of Infectious Cases'

Isoniazid Sensitivity

Annual Mean rates of bacillary cases per 1000 adults from 1961-1968 according to INH-sensitive and INH-resistant strains.

TOWN	"NEW" (Category A)				"OLD" (Category B+C)			
	M+		C+		M+		C+	
	S	R	S	R	S	R	S	R
Kadiri	1.39	0.37	1.32	0.21	1.43	1.50	1.38	0.60
Palmaner	0.84	0.08	0.84	0.08	0.49	0.19	0.55	0.23
Kalahasti	1.52	0.65	1.90	0.35	1.10	1.61	1.22	0.60
Rajampet	1.44	0.72	1.33	0.29	1.32	2.61	1.01	0.85
Chintamani	0.33	0.19	0.52	0.17	0.33	1.26	0.38	0.50
Tiruttani	0.66	0.30	0.93	0.10	0.53	0.90	0.69	0.33
Mean:	1.03	0.39	1.16	0.19	0.87	1.35	0.87	0.52

Note: M+ = Cases positive by microscopy.
C+ = Cases positive by culture only.
S = Isoniazid-sensitive strains.
R = Isoniazid-resistant strains.

Table XXXVII

'Pool of Infectious Cases'

Annual Mean rates of bacillary cases per 1000 adults from 1961-68 in the 6 Towns according to Isoniazid-sensitivity and 'Categories' and methods of sputum examination.

Category	INH-S	%	INH-R	%	Total	%
"NEW" (A)						
M+	1.03	72.5	0.39	27.5	1.42	100.0
C+	1.16	85.9	0.19	14.1	1.35	100.0
all	2.19	79.1	0.58	20.9	2.77	100.0
"OLD" (B+C)						
M+	0.87	39.2	1.35	60.8	2.22	100.0
C+	0.87	62.6	0.52	37.4	1.39	100.0
all	1.74	48.2	1.87	51.8	3.61	100.0
Total	3.93	61.6	2.45	38.4	6.38	100.0

Note: INH-S = Isoniazid-sensitive strains
INH-R = Isoniazid-resistant strains
M+ = Sputum positive by microscopy
C+ = Sputum positive by culture only.

Table XXXVIII

'Pool of Infectious Cases'

Comparison of percentage distribution of mean rates of INH-sensitive and INH-resistant cases per 1000 adults in "INH-PAS" and "INH" towns.

Category	INH-S	%	INH-R	%	Total	%
"NEW" (A)						
INH-PAS	2.63	83.4	0.55	16.6	3.18	100.0
INH	1.78	77.1	0.56	22.9	2.34	100.0
"OLD" (B+C)						
INH-PAS	2.09	57.5	1.55	42.5	3.64	100.0
INH	1.45	40.7	2.13	59.3	3.58	100.0

Table XXXIX

Summary of work done at Surveys I, II & III.

	Total Population	Persons eligible *)	Persons X-rayed No.	Persons X-rayed %	Selected for Bact. Exam.	Examined bacteriologically No.	Examined bacteriologically %	Bacillary Cases No.
Survey I (1960-61)								
Kadiri	16543	9814	8790	89.6	820	711	86.7	89
Palmaner	8812	5156	4675	90.7	275	222	80.7	18
Kalahasthi	23364	15229	12611	82.8	1068	949	88.9	144
Rajampet	10835	6983	6264	89.7	740	608	82.2	65
Chintamani	17438	10400	9343	89.8	608	515	84.7	48
Tiruttani	9079	5839	5077	87.0	413	345	83.5	36
Survey II (1962-64)								
Kadiri	18390	10805	8208	76.0	580	523	90.2	57
Palmaner	10479	6186	5542	89.6	333	300	90.1	23
Kalahasthi	25548	16814	13788	82.0	1396	1233	88.3	221
Rajampet	10686	6857	5096	74.3	469	394	84.0	60
Chintamani	18767	11139	8006	71.9	543	477	87.9	36
Tiruttani	10282	6621	5612	84.8	551	501	90.9	32
Survey III (1965-68) - (a) Treatment Towns.								
Kadiri	20438	12267	10292	83.9	721	666	92.4	107
Palmaner	12148	7471	6396	85.6	380	337	88.7	28
Kalahasthi	29741	19052	16062	84.3	1268	1105	87.2	168
Rajampet	12132	7811	6107	78.2	527	465	88.2	92
Chintamani	20682	12772	10178	79.7	477	431	90.4	47
Tiruttani	12617	8035	6681	83.2	371	304	81.9	51
Survey III (1965-68) - (b) Control Towns.								
Rayachoti	16236	9517	8465	89.0	929	893	96.1	113
Srinivasapur	7968	4610	3857	83.7	211	191	90.5	23
Mulbagal	14587	8127	6686	82.3	337	313	92.9	33
Nagari	7786	4783	4222	88.3	285	267	93.7	41
Puttur	10212	6299	5322	84.5	430	401	93.3	59
Pungamur	16677	10084	8304	82.4	469	433	92.3	53

*) adults (15 years and above).

Table XI

Three Prevalence Surveys

Bacillary Cases per 1000 adult Males or Females

TOWNS	Survey	MALES			FEMALES		
		M+	C+	Total	M+	C+	Total
'TREATMENT' TOWNS							
Kadiri	I	12.0	4.9	16.9	4.3	1.6	5.9
	II	7.8	2.4	10.2	4.3	0.8	5.1
	III	5.9	9.6	15.5	3.2	2.8	6.1
Palmaner	I	6.8	1.2	8.0	1.3	0.5	1.8
	II	1.6	4.0	5.5	1.0	2.8	3.8
	III	5.2	2.5	7.7	0.7	1.6	2.3
Kalahasti	I	13.4	6.1	19.5	4.3	2.3	6.6
	II	9.8	15.9	25.8	3.9	6.1	9.9
	III	9.8	9.5	19.3	3.0	1.5	4.5
Rajampet	I	13.1	3.0	16.2	6.7	2.9	8.9
	II	16.7	5.9	22.7	2.6	1.9	4.6
	III	11.5	15.2	26.7	2.8	4.2	7.0
Chintamani	I	3.0	2.1	5.1	4.4	2.3	6.7
	II	2.5	3.3	5.8	2.3	1.9	4.2
	III	3.7	3.6	7.3	1.2	1.8	3.0
Tiruttani	I	10.5	5.3	15.8	2.2	0.0	2.2
	II	6.5	3.1	9.6	1.2	1.7	2.9
	III	8.4	4.5	12.9	2.5	2.5	5.0
'CONTROL' TOWNS							
Rayachoti	III	8.0	12.9	20.9	2.9	2.9	5.8
Srinivasapur	III	2.9	7.7	10.5	1.2	1.1	2.3
Mulbagal	III	1.9	4.7	6.6	1.0	2.5	3.6
Nagari	III	9.4	9.1	18.4	1.9	0.5	2.3
Puttur	III	11.6	7.3	18.9	1.7	2.9	4.6
Punganur	III	5.2	4.4	9.7	2.6	1.6	4.2

Note: 'M+' denotes positive by Microscopy.

'C+' denotes positive by Culture only.

Table XLI

Three Surveys

Prevalence of bacillary cases per 1000 adult males and females at Surveys I, II & III in the 6 "Treatment" Towns according to sex and method of bacteriological diagnosis.

TOWNS	MALES			FEMALES			BOTH SEXES		
	M+	C+	All	M+	C+	All	M+	C+	All
Survey I (1960-61)									
Kadiri	6.12	2.48	8.60	2.11	0.78	2.89	8.23	3.26	11.48
Palmaner	3.43	0.58	4.00	0.65	0.22	0.87	4.08	0.80	4.88
Kalahasthi	6.70	3.04	9.75	2.16	1.16	3.31	8.86	4.20	13.05
Rajampet	6.66	1.53	8.20	3.29	1.07	4.38	9.95	2.60	12.58
Chintamani	1.53	1.08	2.60	2.15	1.14	3.28	3.68	2.22	5.89
Tiruttani	5.15	2.57	7.73	1.11	0.00	1.12	6.26	2.57	8.85
MEAN	4.93	1.88	6.81	1.91	0.73	2.64	6.84	2.61	9.46
Survey II (1962-64)									
Kadiri	4.01	1.21	5.22	2.08	0.39	2.47	6.09	1.60	7.69
Palmaner	0.78	1.97	2.76	0.48	1.41	1.89	1.26	3.38	4.66
Kalahasthi	4.87	7.89	12.77	1.94	3.07	5.02	6.81	10.96	17.79
Rajampet	8.45	2.95	11.41	1.31	0.96	2.27	9.76	3.91	13.68
Chintamani	1.28	1.71	2.99	1.11	0.93	2.04	2.39	2.64	5.02
Tiruttani	3.24	1.54	4.78	0.58	0.87	1.45	3.82	2.41	6.23
MEAN	3.77	2.88	6.66	1.25	1.27	2.52	5.02	4.15	9.18
Survey III A (1965-68)									
"TREATMENT" TOWNS									
Kadiri	3.03	4.94	7.96	1.59	1.37	2.95	4.62	6.31	10.91
Palmaner	2.54	1.23	3.77	0.33	0.83	1.16	2.87	2.05	4.93
Kalahasthi	4.86	4.73	9.59	1.50	0.77	2.26	6.36	5.50	11.86
Rajampet	5.47	7.25	12.72	1.48	2.17	3.65	6.95	9.42	16.37
Chintamani	1.88	1.86	3.73	0.63	0.87	1.50	2.51	2.73	5.23
Tiruttani	4.21	2.26	6.47	1.23	1.24	2.48	5.44	3.50	8.94
MEAN	3.67	3.71	7.37	1.13	1.21	2.33	4.79	4.92	9.71
Survey III B (1965-68)									
"CONTROL" TOWNS									
Rayachoti	4.12	6.64	10.76	1.41	1.38	2.79	5.53	8.02	13.55
Srinivasapur	1.48	3.96	5.44	0.59	0.54	1.13	2.07	4.50	6.57
Mulbagal	0.97	2.43	3.40	0.50	1.23	1.73	1.47	3.66	5.13
Nagari	4.57	4.42	8.99	0.96	0.23	1.19	5.53	4.65	10.18
Puttur	5.87	3.69	9.56	0.86	1.41	2.27	6.73	5.10	11.83
Punganur	2.63	2.22	4.85	1.29	0.79	2.08	3.92	3.01	6.93
MEAN	3.27	3.89	7.17	0.94	0.93	1.87	4.21	4.82	9.03

Note: M+ denotes cases positive by microscopy.
C+ denotes cases positive by culture only.

Table XLII

Comparisons of Mean Prevalence Rates in the 6 "Treatment" Towns obtained at the 3 consecutive Surveys I, II & III.

Sex	Groups Bact. Diagnosis @)	Mean Prevalence per 1000 adults I	II	III	Changes between Surveys I-II	I-III	P-Values I-II	I-III
Males								
	M+	4.93	3.77	3.67	1.16	1.26*	0.1	0.05
	C+	1.88	2.88	3.71	-1.00	-1.83	>0.2	0.1
	Total	6.81	6.66	7.37	0.15	-0.56	>0.2	>0.2
Females								
	M+	1.91	1.25	1.13	0.66	0.78**	0.08	0.04
	C+	0.73	1.27	1.21	-0.54	-0.48	0.2	0.2
	Total	2.64	2.52	2.33	0.12	0.31	>0.2	>0.2
Both Sexes								
	M+	6.84	5.02	4.79	1.82**	2.05**	0.004	<0.01
	C+	2.61	4.15	4.92	-1.54	-2.31	>0.2	0.06
	Total	9.46	9.18	9.71	0.28	-0.25	>0.2	>0.2

@) Note: M+ = Cases positive by Microscopy.
C+ = Cases positive by Culture only.

Table XLIII

Comparison between Mean Prevalence Rates (per 1000 adults) at Surveys I, II & III in the 3 "INH-PAS" Towns and the 3 "INH" Towns and Mean Changes between Surveys.

Sex	Groups: Bact. diagnosis @)	Mean Prevalence rates: Surveys I	II	III	Changes between Surveys: I-II	I-III	P-Values: I-II	I-III
A. "INH-PAS" TOWNS:								
	Males							
	M+	5.42	3.22	3.48	2.20**	1.94	0.01	>0.05
	C+	2.03	3.69	3.63	-1.66	-1.60	>0.05	>0.05
	All	7.45	6.92	7.11	0.53	0.34	>0.05	>0.05
	Females							
	M+	1.64	1.50	1.14	0.14	0.50*	>0.05	0.03
	C+	0.72	1.62	0.99	-0.90	-0.27	>0.05	>0.05
	All	2.36	3.13	2.12	-0.77	0.24	>0.05	>0.05
	Both Sexes							
	M+	7.06	4.72	4.62	2.34**	2.44	<0.01	0.09
	C+	2.75	5.31	4.62	-2.56	-1.87	>0.2	0.06
	All	9.80	10.05	9.23	-0.24	0.57	>0.2	>0.2
B. "INH" TOWNS:								
	Males							
	M+	4.45	4.32	3.85	0.13	0.60	>0.05	>0.05
	C+	1.73	2.07	3.79	-0.34	-2.06	>0.05	>0.05
	All	6.18	6.39	7.64	-0.21	-1.46	>0.05	>0.05
	Females							
	M+	2.18	1.00	1.11	1.18	1.07	>0.05	>0.05
	C+	0.74	0.92	1.43	-0.18	-0.69	>0.05	>0.05
	All	2.93	1.92	2.54	1.01	0.39	>0.05	>0.05
	Both Sexes							
	M+	6.63	5.32	4.97	1.31	1.66	0.2	0.1
	C+	2.46	2.99	5.22	-0.53	-2.76	>0.2	0.2
	All	9.11	8.31	10.18	0.80	-1.07	>0.2	>0.2

@) Note: M+ = Cases positive by Microscopy.
C+ = Cases positive by Culture only.

Table XLIV

Prevalence of Cases with Isoniazid-sensitive (S) and Isoniazid-resistant (R) strains at Surveys I, II & III - Cases per 1000 adults.

Towns	Males				Females			
	M+		C+		M+		C+	
	S	R	S	R	S	R	S	R
Survey I								
1. Kadiri	5.07	1.04	2.35	0.12	1.81	0.30	0.78	0.00
2. Palmaner	3.43	0.00	0.58	0.00	0.32	0.32	0.22	0.00
3. Kalahasti	5.46	1.24	2.76	0.29	1.12	1.03	0.91	0.25
4. Rajampet	5.77	0.89	0.53	0.00	2.71	0.58	1.07	0.00
5. Chintamani	0.97	0.55	0.81	0.27	1.16	0.99	1.03	0.11
6. Tiruttani	4.58	0.57	2.05	0.51	0.67	0.44	0.00	0.00
Means:	4.21	0.72	1.68	0.20	1.30	0.61	0.67	0.06
Survey II								
1. Kadiri	1.64	2.37	0.94	0.27	1.14	0.95	0.13	0.26
2. Palmaner	0.59	0.20	1.97	0.00	0.48	0.00	0.40	1.00
3. Kalahasti	3.30	1.57	6.28	1.61	0.71	1.24	2.55	0.53
4. Rajampet	4.70	3.76	2.27	0.68	0.79	0.52	0.48	0.48
5. Chintamani	0.48	0.80	0.93	0.78	0.00	1.11	0.40	0.53
6. Tiruttani	2.47	0.76	1.15	0.38	0.39	0.19	0.87	0.00
Means:	2.20	1.58	2.26	0.62	0.59	0.67	0.81	0.47
Survey III A - 'TREATMENT' TOWNS								
1. Kadiri	1.92	1.11	4.53	0.40	1.16	0.42	0.63	0.74
2. Palmaner	2.54	0.00	1.23	0.00	0.33	0.00	0.67	0.17
3. Kalahasti	3.27	1.60	3.67	1.06	1.16	0.34	0.63	0.14
4. Rajampet	2.90	2.56	5.70	1.55	0.84	0.63	1.74	0.43
5. Chintamani	1.18	0.71	1.42	0.44	0.38	0.25	0.70	0.11
6. Tiruttani	3.33	0.88	1.64	0.62	0.70	0.53	1.24	0.00
Means:	2.52	1.14	3.03	0.68	0.76	0.36	0.95	0.27
Survey III B - 'CONTROL' TOWNS								
7. Rayachoti	3.09	1.03	6.28	0.35	0.70	0.70	1.13	0.25
8. Srinivasapur	0.60	0.89	3.11	0.85	0.30	0.30	0.54	0.00
9. Mulbagal	0.65	0.33	1.98	0.46	0.00	0.50	0.77	0.46
10. Nagari	2.28	2.28	4.17	0.25	0.96	0.00	0.23	0.00
11. Puttur	5.06	0.81	3.49	0.21	0.85	0.00	1.21	0.20
12. Punganur	2.10	0.53	2.22	0.00	1.03	0.26	0.56	0.23
Means:	2.30	0.98	3.54	0.35	0.64	0.29	0.74	0.19

Note: M+ = Cases positive by microscopy.
C+ = Cases positive by culture only.
S = Cases with Isoniazid-sensitive strains.
R = Cases with Isoniazid-resistant strains.

Table XLV

Mean prevalence rates per 1000 adults of cases with Isoniazid sensitive strains in the 6 "Treatment" Towns at Surveys I, II & III.

	Surveys			Changes between Surveys		P-Values	
	I	II	III	I - II	I - III	I - II	I - III
A. Cases with INH-Sensitive Strains							
Males							
M+	4.21	2.20	2.52	2.02**	1.69*	< 0.01	< 0.05
C+	1.68	2.26	3.03	-0.58	-1.35	> 0.2	> 0.05
All	5.89	4.45	5.56	1.44	0.34	> 0.1	> 0.2
Females							
M+	1.30	0.59	0.76	0.66	0.54	> 0.1	> 0.1
C+	0.67	0.81	0.95	-0.14	-0.28	> 0.2	> 0.2
All	1.97	1.40	1.71	0.58	0.26	> 0.2	> 0.2
Both Sexes							
M+	5.51	2.78	3.28	2.72**	2.21*	< 0.001	< 0.05
C+	2.35	3.07	3.98	-0.71	-1.62	> 0.2	> 0.05
All	7.86	5.85	7,26	1.85	0.60	> 0.1	> 0.1
B. Cases with INH-Resistant Strains							
Males							
M+	0.72	1.58	1.14	-0.86	-0.43	0.1	0.2
C+	0.20	0.62	0.68	-0.42	-0.48	> 0.2	> 0.2
All	0.91	2.20	1.82	-1.29	-0.91	0.1	> 0.2
Females							
M+	0.61	0.67	0.36	-0.06	0.25	> 0.2	0.2
C+	0.06	0.47	0.27	-0.41*	-0.21	0.03	0.2
All	0.67	1.14	0.63	-0.47*	0.04	0.03	> 0.2
Both Sexes							
M+	1.33	2.25	1.51	-0.93	-0.18	0.1	> 0.2
C+	0.26	1.09	0.94	-0.83	-0.68	0.08	0.1
All	1.58	3.33	2.45	-1.75*	-0.87	0.04	> 0.2

Note: M+ = Cases positive by microscopy.
C+ = Cases positive by culture only.

Table XLVI

Per cent Changes in Prevalences from Survey I (= 100%) to Surveys II & III according to sex, method of demonstrating the bacilli and the bacillary sensitivity to Isoniazid - Rates = Cases per 1000 adult males & females.

Group Sex	Survey I		Survey II		Survey III	
		%		%		%
A. Cases regardless of INH sensitivity						
(1) Cases positive by microscopy (M+)						
Males	4.93	100	3.77	76	3.67	74**
Females	1.91	100	1.25	65**	1.13	59**
Both Sexes	6.84	100	5.02	73**	4.79	70
(2) Cases positive by culture only (C+)						
Males	1.88	100	2.88	153	3.71	197
Females	0.73	100	1.27	174	1.21	166
Both Sexes	2.61	100	4.15	159	4.92	189 1)
(3) All positive cases (M+ & C+)						
Males	6.81	100	6.66	98	7,37	108
Females	2.64	100	2.52	95	2.33	88
Both Sexes	9.46	100	9.18	97	9.71	103
B. Cases with INH-sensitive strains						
(1) Cases positive by microscopy (M+)						
Males	4.21	100	2.20	52**	2.52	60*
Females	1.30	100	0.59	45**	0.76	58*
Both Sexes	5.51	100	2.78	50**	3.28	60*
(2) Cases positive by culture only (C+)						
Males	1.68	100	2.26	135	3.03	180
Females	0.67	100	0.81	121	0.95	142
Both Sexes	2.35	100	3.07	131	3.98	169
(3) All positive cases (M+ & C+)						
Males	5.89	100	4.45	76	5.56	94
Females	1.97	100	1.40	71	1.71	87
Both Sexes	7.86	100	5.85	74	7.26	92
C. Cases with INH-resistant strains						
(1) Cases positive by microscopy (M+)						
Males	0.72	100	1.58	219	1.14	158
Females	0.61	100	0.67	110	0.36	59
Both Sexes	1.33	100	2.25	169	1.51	114
(2) Cases positive by culture only (C+)						
Males	0.20	100	0.62	310*	0.68	340
Females	0.06	100	0.47	783*	0.27	450
Both Sexes	0.26	100	1.09	419 2)	0.94	362
(3) All positive cases (M+ & C+)						
Males	0.91	100	2.20	242*	1.82	200
Females	0.67	100	1.14	170*	0.63	94
Both Sexes	1.58	100	3.33	211*	2.45	155

Note: 1) P = 0.06 2) P = 0.06

Table XLVII

Mean Prevalence Rates at Survey III in the 6 'Treatment' Towns and 6 'Control' Towns (Cases per 1000 adult males & females).

TOWNS	MALES			FEMALES			BOTH SEXES		
	M+	C+	All	M+	C+	All	M+	C+	All
'TREATMENT'	3.66	3.71	7.37	1.13	1.21	2.33	4.79	4.92	9.71
'CONTROLS'	3.27	3.89	7.17	0.93	0.93	1.86	4.21	4.82	9.03
Differences	0.39	-0.18	0.20	0.20	0.28	0.47	0.58	0.10	0.68
S.E. (d.f.10)	0.96	1.15	1.87	0.26	0.29	0.46	1.13	1.32	2.23

Note: M+ = Cases positive by Microscopy.
C+ = Cases positive by Culture only.

Table XLVIII

Comparison of Mean Prevalence Rates at Survey III of cases with Isoniazid sensitive or Isoniazid resistant strains in the 'Treatment' and 'Control' Towns.
Rates = Cases per 1000 adults (Males & Females)

TOWNS	MALES			FEMALES			BOTH SEXES		
	M+	C+	All	M+	C+	All	M+	C+	All
A. Isoniazid Sensitive Strains									
'Treatment'	2.52	3.03	5.55	0.76	0.95	1.71	3.29	3.98	7.26
'Controls'	2.30	3.54	5.84	0.64	0.74	1.38	2.94	4.28	7.22
Differences	0.23	-0.51	-0.29	0.12	0.21	0.33	0.35	-0.31	0.04
S.E.	0.76	1.00	1.43	0.22	0.24	0.32	0.80	1.11	1.30
B. Isoniazid Resistant Strains									
'Treatment'	1.14	0.68	1.82	0.36	0.27	0.63	1.51	0.94	2.45
'Controls'	0.98	0.35	1.33	0.29	0.19	0.48	1.27	0.54	1.82
Differences	0.16	0.33	0.49	0.07	0.08	0.15	0.24	0.40	0.64
S.E.	0.45	0.25	0.65	0.14	0.13	0.23	0.50	0.29	0.73

Note: M+ = Cases positive by Microscopy.
6+ = Cases positive by 6ulture only.

Table XLIX

Mean prevalence of bacillary tuberculosis per 1000 in the 6 'Treatment' Towns as determined by Surveys I, II & III, compared with the annual mean number of sputum-positive cases per 1000 adults on the Register of known cases of tuberculosis - Both sexes.

TOWNS	M+			C+			All positive cases		
	Surveys	'Pool'	RATIO S/P	Surveys	'Pool'	RATIO S/P	Surveys	'Pool'	RATIO S/P
	°/oo	°/oo		°/oo	°/oo		°/oo	°/oo	
Kadiri	6.31	4.91	1.29	3.72	3.46	1.08	10.03	8.37	1.20
Palmaner	2.74	1.61	1.70	2.08	1.70	1.22	4.82	3.31	1.46
Kalahasti	7.34	4.85	1.51	6.89	4.04	1.71	14.23	8.89	1.60
Rajampet	8.89	6.09	1.46	5.31	3.36	1.58	14.21	9.45	1.50
Chintamani	2.86	2.12	1.35	2.53	1.63	1.55	5.38	3.75	1.42
Tiruttani	5.17	2.70	1.91	2.83	1.99	1.42	8.01	4.69	1.71
Mean:	5.55	3.71	1.50	3.89	2.70	1.44	9.44	6.41	1.47
Correlation coefficient r	0.97			0.911			0.95		
P	< 0.01			< 0.02			< 0.01		

Note: M+ = Cases positive by microscopy
C+ = Cases positive by culture only.

Table L

Tuberculin Sample Survey 1966-69

Coverage by Tuberculin Testing

TOWNS	Persons[1)] living in the sample blocks No.	Died, moved out or absent No.	Available for testing No.	Tested No.	Tested & read No.
Kadiri	2207	717	1490	1044	882
Palmaner	2234	554	1680	1406	1336
Kalahasti	3109	720	2389	1733	1546
Rajampet	1922	273	1649	921	781
Chintamani	2269	580	1689	1315	1204
Tiruttani	1990	365	1625	1222	1144
Rayachoti	2431	436	1995	1303	1273
Srinivasapur	2473	642	1831	1323	1210
Mulbagal	2590	641	1949	1351	1227
Nagari	2083	457	1626	1390	[illegible]

Table LI

Tuberculin Sample Survey 1966-69

Mean percentage of reactors to PPD-S (⩾ 8 mm) according to Age.

Town	2-4 years		5-9 years		10-14 years		15-19 years	
	Tested No.	Reactors %	Tested No.	Reactors %	Tested No.	Reactors %	Tested No.	Reactors %
Kadiri	98	8.1	124	19.5	140	35.4	72	65.3
Palmaner	185	2.6	213	8.4	203	16.9	133	19.5
Kalahasti*)	152	11.2	233	26.2	196	42.3	157	56.1
Rajampet	66	20.5	89	33.7	76	45.6	64	59.8
Chintamani	196	6.5	213	12.5	178	25.8	129	40.0
Tiruttani	119	8.6	141	9.0	117	38.5	103	44.2
Rayachoti	123	8.3	214	19.4	196	40.2	109	51.2
Srinivasapur	176	2.9	235	11.0	213	14.7	89	36.6
Mulbagal	175	1.4	236	7.2	239	18.7	108	21.6
Nagari	146	8.2	194	15.7	182	36.9	103	52.8
Puttur	129	3.3	225	13.8	193	31.2	91	65.1
Punganur	192	2.9	248	16.0	176	26.1	107	38.2

Town	20-24 years		25-34 years		35-44 years		45-54 years		55+ years	
	Tested No.	Reactors %	Tested No.	Reactors %	Tested No.	Reactors %	Tested No.	Reactors %	Tested No.	Reactors %
Kadiri	42	73.3	145	71.3	120	82.0	73	83.1	68	76.7
Palmaner	95	35.5	180	58.9	137	51.7	103	57.5	87	63.2
Kalahasti*)	110	62.8	268	82.3	217	79.0	118	74.5	95	79.7
Rajampet	41	58.6	151	82.4	136	84.4	81	81.7	77	76.4
Chintamani	74	40.4	147	56.5	127	65.5	71	64.6	69	69.3
Tiruttani	104	54.4	218	66.4	156	68.6	105	69.4	81	65.1
Rayachoti	94	63.5	222	69.1	131	76.7	95	78.6	89	71.0
Srinivasapur	63	44.3	149	51.3	120	70.8	91	66.2	74	53.8
Mulbagal	71	29.6	137	52.8	113	65.4	77	60.8	71	59.5
Nagari	97	59.0	197	66.3	181	71.2	127	70.4	77	77.6
Puttur	82	46.3	207	66.5	177	73.9	93	76.0	66	63.4
Punganur	105	60.0	207	62.3	139	70.7	84	48.3	74	56.6

*) Data based upon 15 sample blocks

Table LII

Tuberculin Sample Survey 1966-69

Comparison of Mean Percentages of tuberculin reactors ($\geq$8 mm) in the "Treatment" and "Control" Towns.

Age Group	Treatment Towns	Control Towns	Difference
2- 4	9.60	4.49	5.11**
5- 9	18.21	13.85	4.36**
10-14	34.06	27.98	6.08
15-19	47.48	44.26	3.22
20-24	54.16	50.45	3.71**
25-34	69.63	61.38	8.25
35-44	71.87	71.45	0.42
45-54	71.80	66.72	5.08**
55+	71.25	63.65	8.10

Table LIII

Comparison of the results of tuberculin testing during 1959 and 1966-69.

Towns	1959 Survey 5-9 years	1966-69 Survey 5-9 years	Difference
	%	%	%
A. "Treatment" Group			
Kadiri	23.4	19.5	3.9
Rajampet	20.7	33.7	-13.0
Chintamani	18.5	12.5	6.0
Tiruttani	3.4	8.9	-5.5
Kalahasti	21.9	26.2	-4.3
Palmaner	6.2	8.4	-2.2
Means:	15.68	18.20	-2.52
B. "Control" Group			
Rayachoti	15.4	19.4	-4.0
Srinivasapur	13.5	11.0	-2.5
Mulbagal	7.4	7.2	0.2
Nagari	15.6	15.7	-0.1
Puttur	19.5	13.8	5.7
Punganur	12.1	16.0	-3.9
Means:	13.92	13.85	0.07

Appendix Table I

1959 Sample Survey

Frequency distribution of diameters of induration to Mantoux Tests among school children in Standards I & II (excluding children with BCG vaccination scars).

Diameters of Indurations mm	Kadiri	Rayachoti	Rajampet	Chintamani	Srinivasapur	Mulbagal
0-	145	200	102	78	83	109
2-	73	71	61	281	86	134
4-	24	9	9	51	4	6
6-	9	2	3	15	1	3
8-	12	2	4	9	2	1
10-	13	3	10	12	1	1
12-	9	12	10	14	6	2
14-	8	12	11	16	4	4
16-	3	9	1	8	5	1
18-	8	9	2	7	4	4
20-	7	1	3	4	1	3
22-	4	-	1	4	2	1
24+	1	1	-	4	1	-
Total	316	331	217	503	200	209

Diameters of Indurations mm	Tiruttani	Nagari	Pattur	Kalahasti	Palmaner	Punganur
0-	28	34	12	175	96	142
2-	104	99	147	228	84	37
4-	11	24	23	17	3	3
6-	5	5	5	7	-	1
8-	-	2	-	9	3	5
10-	-	3	3	12	2	4
12-	-	-	-	16	1	1
14-	-	3	9	22	2	2
16-	-	-	5	9	-	3
18-	-	7	5	13	2	5
20-	-	8	10	23	2	4
22-	-	1	3	7	-	-
24+	-	-	4	-	-	-
Total	148	186	226	538	195	207

Appendix Table II

Per cent cases treated per month - First Year

	KADIRI				PALMANER			
	Males		Females		Males		Females	
	M+	C+	M+	C+	M+	C+	M+	C+
Cases No.	141	132	70	53	31	31	14	19
Months								
0	96.3	86.7	96.9	94.1	93.1	96.7	100.0	89.5
1	92.5	84.4	95.2	90.2	92.9	93.3	100.0	83.3
2	91.5	80.5	95.2	90.0	92.9	93.3	100.0	72.2
3	89.9	75.8	95.2	88.0	85.7	93.1	100.0	66.7
4	89.0	73.4	95.1	86.0	85.7	93.1	100.0	66.7
5	87.2	72.4	93.4	85.1	85.2	93.1	100.0	66.7
6	84.0	68.8	93.2	78.7	85.2	93.1	100.0	58.8
7	84.0	66.4	93.2	78.7	85.2	86.2	100.0	58.8
8	84.0	63.2	91.5	74.5	80.8	86.2	92.3	58.8
9	78.9	61.6	88.1	72.3	80.8	82.8	84.6	58.8
10	76.0	66.0	86.4	70.2	80.8	82.8	76.9	58.8
11	75.8	56.1	83.1	68.1	76.9	75.9	69.2	58.8
12	75.6	52.9	82.8	66.0	76.0	72.4	61.5	58.8

	KALAHASTI				RAJAMPET			
	181	235	56	82	113	107	43	29
0	91.1	73.9	86.0	76.6	94.2	79.8	91.9	92.9
1	89.7	69.6	85.7	71.8	90.2	78.9	88.9	82.1
2	82.9	66.2	85.7	69.6	81.6	74.0	85.7	78.6
3	80.4	62.8	83.7	65.2	80.4	69.2	82.9	78.6
4	76.0	58.4	81.6	65.2	77.1	66.0	79.4	78.6
5	74.5	54.7	81.6	63.8	74.5	63.4	78.1	77.8
6	72.5	52.8	79.2	60.9	73.4	60.0	78.1	74.1
7	71.1	50.7	77.1	56.5	71.7	58.0	75.0	70.4
8	68.8	46.0	74.5	56.5	71.4	57.0	75.0	66.7
9	67.4	44.6	70.2	55.1	70.0	50.5	75.0	63.0
10	67.4	40.9	69.6	55.1	64.0	49.5	71.9	57.7
11	63.1	38.7	67.4	53.6	61.4	47.5	70.0	50.0
12	61.4	36.1	65.2	52.2	60.5	44.9	69.0	46.2

	CHINTAMANI				TIRUTTANI			
	35	56	34	37	42	38	12	14
0	81.8	73.1	87.5	70.6	83.8	70.6	81.8	40.0
1	81.8	71.2	87.5	64.7	83.3	70.6	81.8	40.0
2	77.4	69.2	87.5	64.7	80.6	70.6	81.8	40.0
3	76.7	63.5	83.3	63.6	80.6	70.6	81.8	40.0
4	73.3	61.5	83.3	57.6	77.8	67.7	81.8	40.0
5	66.7	58.8	83.3	51.5	74.3	64.7	81.8	40.0
6	63.3	52.9	80.0	46.9	73.5	58.8	60.0	40.0
7	63.3	52.9	79.3	43.8	73.5	55.9	60.0	40.0
8	63.3	52.9	75.9	43.8	68.8	55.9	60.0	40.0
9	60.0	52.9	75.9	43.8	68.8	55.9	60.0	33.3
10	53.3	51.0	71.4	43.8	61.3	52.9	60.0	33.3

Appendix Table III

Percentage of cases treated per month - according to the period of diagnosis.*)

	Sy. I	Interval between Sys. I & II	Sy. II	Interval between Sys.II & III	Sy. III
			KADIRI		
Cases No.	85	44	41	92	66
Months					
0	96.5	86.4	97.6	95.7	87.9
1	96.5	81.8	89.7	95.7	80.3
2	95.2	79.1	89.5	94.5	77.3
3	95.2	79.1	84.2	92.3	69.7
4	95.1	79.1	84.2	89.0	69.7
5	93.8	76.2	83.8	87.6	69.2
6	92.4	75.0	78.4	86.4	64.6
7	89.9	72.5	78.4	84.1	64.6
8	88.6	67.5	78.4	84.1	61.5
9	84.6	62.5	75.7	82.8	58.5
10	82.1	61.5	69.4	81.6	55.4
11	82.1	59.0	61.8	79.3	54.7
12	81.3	56.4	55.9	79.1	52.4
Means:	90.3	72.0	79.0	87.1	66.6
			KALAHASTI		
Cases No.	118	102	173	125	-
Months					
0	82.2	81.4	84.4	73.6	
1	82.1	81.4	78.6	69.7	
2	75.9	78.0	74.9	67.5	
3	71.9	75.0	70.0	67.0	
4	71.0	73.0	65.1	62.1	
5	69.3	72.0	62.1	59.1	
6	67.9	69.7	59.8	58.4	
7	65.2	64.7	58.0	56.3	
8	63.1	60.2	55.7	52.3	
9	60.4	57.1	53.9	51.4	
10	60.4	55.1	51.5	49.5	
11	57.7	52.0	49.1	46.3	
12	56.9	49.0	47.0	43.5	
Means:	68.0	66.8	62.3	58.2	

*) Data from Palmaner and Tiruttani are omitted as the No. of cases were too few.

Appendix Table III contd...

Percentage of cases treated per month according to the period of diagnosis.

	Sy. I	Interval between Sys. I & II	Sy. II	Interval between Sys. II & III	Sy. III
			RAJAMPET		
Cases No.	56	32	42	62	65
Months					
0	98.2	87.5	92.9	87.1	76.5
1	98.2	87.1	90.5	85.5	66.2
2	98.2	80.0	77.5	82.0	59.1
3	98.2	76.7	77.5	78.7	53.9
4	98.2	75.9	76.9	72.1	49.2
5	98.1	75.9	76.3	65.0	47.6
6	98.1	72.4	71.1	65.0	44.4
7	90.4	72.4	69.4	65.0	44.4
8	88.5	72.4	68.6	63.3	44.4
9	82.4	69.0	65.7	59.3	44.4
10	76.0	67.9	62.9	57.6	41.3
11	74.0	67.9	55.9	54.2	38.7
12	72.9	66.7	50.0	53.5	37.1
Means:	90.1	68.6	71.9	68.3	49.8
			CHINTAMANI		
Cases No.	46	26	17	27	26
Months					
0	91.3	96.2	82.4	81.5	38.5
1	89.1	92.3	76.5	81.5	38.5
2	88.9	92.3	76.5	81.5	32.0
3	86.7	92.0	70.6	80.8	21.7
4	84.4	88.0	70.6	76.9	17.4
5	77.8	87.5	64.7	76.9	13.0
6	75.0	75.0	58.8	73.1	13.0
7	74.4	70.8	58.8	73.1	13.0
8	74.4	66.7	58.8	73.1	13.0
9	74.4	62.5	58.8	73.1	13.0
10	69.1	62.5	52.9	69.2	13.0
11	64.3	62.5	52.9	69.2	13.0
12	61.9	58.3	52.9	68.0	13.0
Means:	77.8	77.4	64.2	75.2	19.4

APPENDIX TABLE IV

Treatment Results at the end of one year

A. M A L E S

Towns	Cases	Died	Moved out	TB positive cases			TB–	NE
				S	R	N		
	No.	No.	No.	No.	No.	No.	No.	No.
a. Isoniazid sensitive cases								
(i) M+								
Kadiri	99	11	5	13	16	1	48	5
Palmaner	22	2	1	1	3	0	15	0
Kalahasti	99	13	2	17	13	2	45	7
Rajampet	67	10	4	11	17	0	23	2
Chintamani	17	1	1	4	5	0	7	0
Tiruttani	22	2	2	2	7	0	8	1
(ii) C+								
Kadiri	101	3	3	27	5	1	55	7
Palmaner	29	1	0	5	0	0	23	0
Kalahasti	137	8	4	25	8	3	78	11
Rajampet	75	5	3	16	11	0	34	6
Chintamani	27	2	1	8	4	0	9	3
Tiruttani	22	1	0	7	1	0	13	0
b. Isoniazid resistant cases								
(i) M+								
Kadiri	17	4	1	1	7	0	4	0
Palmaner	1	0	0	0	1	0	0	0
Kalahasti	32	6	1	1	19	0	3	2
Rajampet	24	7	3	0	12	0	1	1
Chintamani	8	0	1	0	6	0	1	0
Tiruttani	4	2	0	0	1	0	1	0
(ii) C+								
Kadiri	7	1	0	2	0	0	4	0
Palmaner	0	0	0	0	0	0	0	0
Kalahasti	22	3	1	1	3	0	11	3
Rajampet	8	1	0	0	5	0	2	0
Chintamani	10	0	0	0	5	0	5	0
Tiruttani	3	0	0	0	1	0	2	0
c. Sensitivity test not done								
(i) M+								
Kadiri	14	0	1	1	1	1	8	2
Palmaner	4	0	0	0	0	0	3	1
Kalahasti	12	2	1	1	2	1	5	0
Rajampet	6	0	0	1	1	0	4	0
Chintamani	2	1	0	0	0	0	1	0
Tiruttani	5	1	1	1	1	0	1	0
(ii) C+								
Kadiri	3	0	0	0	0	0	3	0
Palmaner	0	0	0	0	0	0	0	0
Kalahasti	2	0	1	0	0	0	1	0
Rajampet	0	0	0	0	0	0	0	0
Chintamani	1	0	0	0	0	0	1	0
Tiruttani	0	0	0	0	0	0	0	0

NOTE: M+ = Cases initially positive by microscopy.
C+ = Cases initially positive by culture only
S = Cases with Isoniazid-sensitive strains initially
R = Cases with Isoniazid-resistant strains initially
N = Sensitivity Test not available

Appendix Table IV contd.....

B. F E M A L E S

Towns	Cases No.	Died No.	Moved out No.	TB positive cases S No.	R No.	N No.	TB- No.	NE No.
a. Isoniazid sensitive cases								
(i) M+								
Kadiri	45	3	2	4	6	2	27	1
Palmaner	9	0	0	0	2	0	7	0
Kalahasti	20	2	0	3	3	1	10	1
Rajampet	25	3	0	1	9	1	9	2
Chintamani	14	0	1	0	3	0	8	2
Tiruttani	5	2	0	0	1	0	2	0
(ii) C+								
Kadiri	39	2	1	2	4	0	28	2
Palmaner	13	1	0	2	0	0	9	1
Kalahasti	40	1	0	4	3	0	28	4
Rajampet	21	0	0	4	3	0	13	0
Chintamani	18	1	0	3	1	0	11	2
Tiruttani	4	1	0	0	0	0	3	0
b. Isoniazid reistant cases								
(i) M+								
Kadiri	10	0	2	0	2	0	6	0
Palmaner	2	0	0	0	0	0	1	1
Kalahasti	20	2	1	1	10	1	4	1
Rajampet	7	3	2	0	2	0	0	0
Chintamani	8	2	1	0	4	0	1	0
Tiruttani	3	0	0	0	3	0	0	0
(ii) C+								
Kadiri	8	1	0	0	4	0	3	0
Palmaner	4	1	1	0	1	0	1	0
Kalahasti	14	2	0	0	5	1	5	1
Rajampet	4	1	0	0	2	0	1	0
Chintamani	6	0	2	0	2	0	2	0
Tiruttani	0	0	0	0	0	0	0	0
c. Sensitivity test not done								
(i) M+								
Kadiri	7	1	0	0	1	1	4	0
Palmaner	2	0	0	0	1	0	1	0
Kalahasti	3	0	0	0	0	0	2	1
Rajampet	2	0	0	1	1	0	0	0
Chintamani	6	0	0	2	1	0	3	0
Tiruttani	1	0	0	0	0	0	1	0
(ii) C+								
Kadiri	1	0	0	0	0	0	1	0
Palmaner	0	0	0	0	0	0	0	0
Kalahasti	2	0	1	1	0	0	0	0
Rajampet	1	0	1	0	0	0	0	0
Chintamani	0	0	0	0	0	0	0	0
Tiruttani	0	0	0	0	0	0	0	0

NOTE: M+ = Cases initially positive by microscopy
C+ = Cases initially positive by culture only
S = Cases with Isoniazid-sensitive strains initially
R = Cases with Isoniazid-resistant strains initially
N = Sensitivity Test not available
NE = Sputum not examined

Appendix Table V

5-years' Follow-up Study

All Towns

Follow-up results of treated cases according to Age and Method of initial Bacteriological Diagnosis
Both Sexes

Year of Observation	Positive by Microscopy			Positive by culture only		
	Died %	TB+ %	TB- %	Died %	TB+ %	TB- %
15-24 years						
Initial No. of cases	106			61		
1	9.0	37.0	54.0	7.0	24.2	68.8
2	14.6	34.2	51.2	10.8	19.8	69.4
3	16.9	29.4	53.7	13.0	21.2	65.8
4	19.7	19.7	60.6	16.3	3.8	79.9
5	25.3	26.2	48.5	20.7	9.3	70.0
25-34 years						
Initial No. of cases	190			147		
1	10.7	43.4	45.9	1.4	31.9	66.7
2	21.1	35.9	43.0	5.9	32.9	61.2
3	28.8	28.6	42.6	9.2	25.3	65.5
4	34.3	23.7	42.0	11.1	24.9	64.0
5	37.9	20.7	41.4	14.2	26.4	59.4
35-44 years						
Initial No. of cases	150			148		
1	12.0	40.2	47.8	5.5	34.0	60.5
2	22.1	37.7	40.2	13.7	31.9	54.4
3	31.1	28.3	40.6	19.7	28.2	52.1
4	38.2	24.1	37.7	27.3	15.7	57.0
5	41.8	20.6	37.6	30.2	14.0	55.8
45-54 years						
Initial No. of cases	94			116		
1	18.9	45.1	36.0	9.8	37.6	52.6
2	28.1	43.9	28.0	18.0	28.8	53.2
3	39.1	28.5	32.4	24.8	25.8	49.4
4	47.0	24.4	28.6	28.1	24.4	47.5
5	54.8	22.6	22.6	32.3	10.7	57.0
55+ years						
Initial No. of cases	63			81		
1	14.8	44.3	40.9	12.8	30.9	56.3
2	35.2	36.2	28.6	20.8	26.4	52.8
3	47.8	23.4	28.8	32.4	24.7	42.9
4	49.8	17.5	32.7	46.2	15.9	37.9
5	58.6	19.6	21.8	46.2	17.0	36.8

Appendix Table VI

Deaths due to all causes and among bacillary cases of tuberculosis

Age Group	Males			Females		
	Person Years	Deaths		Person Years	Deaths	
		Due to all causes No.	Among bacillary cases No.		Due to all causes No.	Among bacillary cases No.
KADIRI						
0-	19793	146	-	18459	170	-
15-	7838	21	3	8480	33	1
25-	8155	30	5	7899	39	5
35-	5675	47	11	4144	25	3
45-	3022	68	12	3255	40	2
55+	3096	137	14	2929	109	3
all	47579	449	45	45166	416	14
PALMANER						
0-	13388	64	-	13338	80	-
15-	5274	23	-	5262	25	2
25-	4691	21	-	5164	18	1
35-	3860	22	2	3544	14	-
45-	2747	41	3	2671	23	3
55+	2141	121	3	2140	90	1
all	32101	292	10	32119	250	7
KALAHASTI						
0-	29230	134	-	27087	156	-
15-	14743	71	12	14301	82	5
25-	14678	134	35	14847	92	13
35-	10825	179	37	9837	79	13
45-	6452	186	39	8059	124	9
55+	5408	364	46	5819	302	3
all	81336	1068	169	79950	835	43

contd.....

Appendix Table VI contd.....

Deaths due to all causes and among the bacillary cases of tuberculosis

Age Group	Males			Females		
	Person Years	Deaths		Person Years	Deaths	
		Due to all causes No.	Among bacillary cases No.		Due to all causes No.	Among bacillary cases No.
RAJAMPET						
0-	11198	51	-	10626	52	-
15-	5470	31	5	5005	44	4
25-	5132	47	9	5341	35	9
35-	4091	55	14	3615	29	5
45-	2670	72	16	2945	56	6
55+	2299	146	18	2382	132	5
all	30860	402	62	29914	348	29
CHINTAMANI						
0-	22923	167	-	22647	129	-
15-	10075	32	-	9667	41	5
25-	9722	40	5	8990	26	10
35-	5545	35	1	6096	30	3
45-	4362	53	4	4262	55	1
55+	3597	179	2	3191	137	2
all	56224	506	12	54853	418	21
TIRUTTANI						
0-	11532	76	-	10850	69	-
15-	4862	23	3	5026	22	1
25-	5502	29	5	6070	31	5
35-	4249	71	10	3829	39	-
45-	2724	60	10	3087	50	4
55+	2235	138	12	1945	107	2
all	31104	397	40	30807	318	12

Appendix-Table VII

'Pool of Infectious Cases'

Yearly distribution of cases on the Register of each town according to result of sputum examinations in each calendar year and categories*) A, B & C indicating period of first bacteriological diagnosis.

Town	Year	Cases on Register No.	Cases on Register °/oo **)	Sputum examinations: Positive Cat.A M	Positive Cat.A F	Positive Cat.B M	Positive Cat.B F	Positive Cat.C M	Positive Cat.C F	Negative M	Negative F	Not done M	Not done F
Kadiri	1960	109	10.5	72	26	3	0	0	0	4	2	1	1
	61	121	11.4	14	6	32	7	3	1	31	16	9	2
	62	176	16.4	44	24	6	2	27	8	39	15	7	4
	63	183	15.5	15	9	22	6	22	7	53	30	15	4
	64	198	17.4	26	11	6	2	33	11	57	35	13	4
	65	204	17.2	19	6	12	3	27	12	66	37	17	5
	66	283	22.9	62	31	12	2	41	13	60	41	17	4
	67	282	22.3	12	7	21	10	32	11	93	49	35	12
	68	280	21.6	11	9	7	2	49	15	98	58	25	6
Palmaner	1960	-	-	-	-	-	-	-	-	-	-	-	-
	61	22	4.1	11	7	0	0	0	0	2	0	1	1
	62	25	4.4	3	2	2	1	0	0	10	6	1	0
	63	41	6.8	12	6	0	1	4	1	10	6	1	0
	64	56	8.9	8	7	5	4	3	3	15	6	4	1
	65	53	8.0	6	0	5	2	8	3	16	10	1	2
	66	52	7.5	1	2	3	0	8	3	18	9	6	2
	67	50	6.9	1	1	0	1	8	2	22	11	3	1
	68	76	10.0	19	9	0	0	9	2	19	13	4	1
Kalahasti	1960	-	-	-	-	-	-	-	-	-	-	-	-
	61	168	11.1	95	28	0	0	7	5	10	6	15	2
	62	179	11.3	38	10	41	13	6	3	39	13	11	6
	63	196	12.0	29	13	12	4	38	9	49	21	16	5
	64	387	22.8	156	59	11	3	42	7	59	30	16	4
	65	412	23.4	42	9	82	24	53	7	108	50	26	11
	66	376	20.6	11	4	13	2	67	15	118	46	72	29
	67	353	18.7	10	1	5	1	75	23	116	45	58	18
	68	406	20.8	64	27	4	0	53	14	124	47	51	22

cont.....

Appendix Table VII contd.....

Town	Year	Cases on Register		Sputum examinations									
				Positive						Negative		Not done	
				Cat.A.		Cat.B		Cat.C					
		No.	°/oo	M	F	M	F	M	F	M	F	M	F
Rajampet													
	1960	73	10.4	35	25	6	1	0	0	3	2	1	0
	61	86	12.4	15	5	13	11	5	1	21	11	3	1
	62	110	16.0	34	6	5	2	15	6	19	10	9	4
	63	129	18.3	28	6	22	3	20	3	20	11	10	6
	64	131	17.9	15	5	15	5	34	5	25	10	14	3
	65	118	15.5	14	1	7	0	31	5	31	12	11	6
	66	167	21.3	46	13	5	1	25	3	39	12	19	4
	67	179	22.1	20	9	28	7	25	2	40	16	27	5
	68	157	18.8	5	2	5	2	31	7	50	17	30	8
Chintamani													
	1960	49	4.7	19	24	0	1	0	0	1	3	0	1
	61	61	5.7	5	8	9	9	0	2	11	16	0	1
	62	65	6.0	7	5	3	4	7	8	7	18	5	1
	63	84	7.5	16	8	3	2	10	11	13	15	2	4
	64	96	8.4	12	5	10	5	14	9	16	19	2	4
	65	94	7.8	3	0	6	0	22	13	21	20	3	6
	66	90	7.2	4	1	0	0	19	6	25	19	7	9
	67	116	9.1	21	15	3	1	16	5	25	18	7	5
	68	109	8.3	3	1	13		16	3	28	23	12	6
Tiruttani													
	1960	39	6.6	28	5	4	0	0	0	1	0	1	0
	61	40	6.5	3	2	12	4	4	0	10	1	4	0
	62	40	6.3	8	0	0	0	11	1	9	1	7	3
	63	65	9.7	22	12	3	0	10	1	12	2	2	1
	64	68	9.7	8	5	12	5	8	0	15	5	8	2
	65	59	8.0	3	0	5	1	17	4	16	8	4	1
	66	55	7.1	2	1	1	0	11	1	17	6	12	4
	67	71	6.7	14	7	1	0	8	4	16	6	15	0
	68	90	10.6	24	10	5	4	6	1	22	8	7	3

Note: *) Initial bacteriological diagnosis done:-

(i) the same year - Category A.
(ii) the previous calendar year - Category B.
(iii) earlier than the previous calendar year - Category C.

**) Cases per 1000 adults.

Appendix Table VIII

'Pool of Infectious Cases'

Percentage of Isoniazid-resistant cases in categories 'A' ("NEW") & 'B+C' ("OLD") in 'Two-drugs Towns' versus 'One-drug Towns' among total positive cases on the register each year from 1961-1968.

Year	INH-PAS Towns			INH Towns		
	Total per 1000	INH-R Cases		Total per 1000	INH-R Cases	
		No.	%		No.	%
"NEW" (A)						
1961	4.44	0.80	18.0	1.63	0.31	19.0
62	3.39	0.65	19.2	2.72	0.69	25.4
63	2.54	0.51	20.1	3.00	1.10	27.5
64	6.13	1.23	20.1	2.03	0.54	26.6
65	1.97	0.25	12.7	0.90	0.21	23.3
66	2.90	0.49	16.9	2.76	0.71	25.7
67	0.80	0.11	13.8	3.00	0.71	23.7
68	3.30	0.39	11.8	1.70	0.20	11.8
Mean:	3.18	0.55	16.58	2.34	0.56	22.88
"OLD" (B+C)						
1961	1.64	0.58	35.4	3.17	2.00	63.1
62	2.84	1.30	45.8	2.67	1.92	71.9
63	3.32	1.52	45.8	3.74	2.49	66.6
64	3.56	1.74	48.9	5.00	3.34	66.8
65	5.57	2.31	41.5	4.27	2.50	58.5
66	4.27	1.44	33.7	2.66	1.43	53.8
67	4.30	1.88	43.7	3.77	1.83	48.5
68	3.57	1.61	45.1	3.37	1.53	45.4
Mean:	3.64	1.55	42.49	3.58	2.13	59.33

Appendix Table IX

'Pool of Infectious Cases'

Rate of sputum positive cases (both sexes) per 1000 adults according to sputum examinations each calendar year (regardless of Cat.A, B & C)

Years	Kadiri		Palmaner		Kalahasti		Rajampet		Chintamani		Tiruttani	
	M+	C+	M+	C+	M+	C+	M+	C+	M+	C+	M+	C+
1960	6.63	3.08	–	–	–	–	7.13	2.43	2.22	2.03	4.75	1.52
61	3.40	2.55	2.76	0.55	5.94	2.97	4.32	2.88	1.78	1.31	2.60	1.46
62	6.60	3.72	0.70	0.70	3.94	2.62	7.56	2.33	1.83	1.28	2.03	1.10
63	4.33	2.98	1.98	1.99	3.24	3.18	9.08	2.55	2.41	2.05	3.74	3.44
64	3.60	4.22	1.11	3.65	7.01	9.36	6.15	4.64	3.04	1.74	7.56	2.84
65	3.63	3.04	1.06	2.57	6.07	6.24	4.21	3.42	1.83	2.00	1.62	2.43
66	6.64	6.39	0.86	1.58	3.40	2.74	6.62	5.22	1.44	0.96	1.03	1.03
67	4.98	2.37	0.96	0.83	3.66	2.44	5.19	5.06	2.58	2.19	2.09	2.09
68	4.40	2.78	3.42	1.71	5.54	2.77	4.56	1.68	1.99	1.07	3.88	2.00
Means:	4.91	3.46	1.61	1.70	4.85	4.04	6.09	3.36	2.12	1.63	2.70	1.99

Note: M+ = Cases positive by microscopy

C+ = Cases negative by microscopy but positive by culture.

Appendix Table X

(a) Time Table for the three consecutive the 6 'Treatment' Towns.

Towns	Survey I *)	Survey II	Survey III
Kadiri	1960, March-Aug.	1962, Jan.-July	1965, Sep.-'66 Apr.
Rajampet	1960, March-July	1962, Jan.-Nov.	1966, July-'67 Jan.
Chintamani	1960, July-'61 Jan.	1962, Dec.-'63 Sep.	1966, Dec.-'67 Nov.
Tiruttani	1960, Aug.-Dec.	1963, Jan.-July	1967, July-'68 Feb.
Palmaner	1960, Nov.-'61 March	1963, Sep.-'64 Jan.	1967, Dec.-'68 May
Kalahasti	1961, Apr.-Dec.	1963, Sep.-'64 Oct.	1968, Apr.-'69 Jan.

*) Note: "Survey I" relates to the survey of the remaining portion (75-80%) of the Towns not covered by the 1959 Sample Survey.

(b) Mean intervals in months between Surveys.

Towns	Intervals in months		
	Sy.I - Sy.II	Sy.II - Sy.III	Sy.I - Sy.III
Kadiri	22.5	44.5	67
Rajampet	27.5	49.5	77
Chintamani	30.5	49.0	79.5
Tiruttani	30.0	54.5	84.5
Palmaner	34.0	51.5	85.5
Kalahasti	31.5	53.0	84.5
Means:	29.3	50.3	79.7

(c) Time Table for "Survey III" of the 6 'Control' Towns.

Towns	"Survey III"
Rayachoti	1965, May-August
Srinivasapur	1966, March-July
Mulbagal	1966, August-December
Nagari	1967, March-June
Puttur	1968, November-'68 March
Punganur	1968, May-October

Appendix Table XI

Basic data obtained at Prevalence Surveys I, II & III.

1. K A D I R I

Survey	Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
						M+	C+
			M a l e s				
I	15–24	1445	1251	49	41	7	2
	25–34	1395	1264	104	92	10	3
	35–44	973	902	132	114	18	5
	45–54	575	503	94	85	8	6
	55+	602	530	142	122	4	3
	No data	0	0	0	0	0	1
II	15–24	1538	1141	37	34	4	1
	25–34	1649	1259	95	87	8	3
	35–44	1146	915	96	87	9	2
	45–54	580	447	62	55	5	1
	55+	606	427	77	70	4	2
	No data	0	0	0	0	0	0
III	15–24	2002	1692	38	38	3	3
	25–34	1549	1224	76	69	3	9
	35–44	1266	1184	127	117	11	18
	45–54	860	786	92	87	5	11
	55+	623	507	120	109	8	8
	No data	0	0	0	0	0	0
			F e m a l e s				
I	15–24	1597	1424	47	39	4	0
	25–34	1326	1250	69	62	4	3
	35–44	708	659	50	44	4	1
	45–54	621	561	58	46	2	1
	55+	572	446	75	66	2	1
	No data	0	0	0	0	0	0
II	15–24	1712	1243	41	36	3	0
	25–34	1585	1302	70	62	6	2
	35–44	807	664	31	26	2	1
	45–54	613	455	33	31	1	0
	55+	569	355	38	35	3	0
	No	0	0	0	0	0	0
III	15–24	1686	1292	31	27	4	1
	25–34	1781	1563	72	67	7	9
	35–44	1070	972	59	57	3	1
	45–54	521	431	44	40	1	0
	55+	909	641	62	55	0	2
	No data	0	0	0	0	0	0

Contd.....

Appendix Table XI Contd.....

2. P A L M A N E R

Survey	Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
						M+	C+
			M a l e s				
I	15–24	710	621	24	20	0	0
	25–34	609	554	29	21	3	0
	35–44	518	481	31	23	4	1
	45–54	390	354	35	27	3	0
	55+	355	301	41	32	2	1
	No data	2	1	0	0	0	0
II	15–24	897	769	36	31	0	1
	25–34	802	729	38	32	1	1
	35–44	624	575	42	41	0	3
	45–54	433	398	47	44	2	2
	55+	329	292	36	33	1	0
	No data	5	4	1	1	0	0
III	15–24	1136	896	24	21	4	0
	25–34	890	757	33	29	2	1
	35–44	634	564	41	35	2	2
	45–54	557	459	45	42	3	1
	55+	442	381	59	52	3	3
	No data	0	0	0	0	0	0
			F e m a l e s				
I	15–24	660	595	13	9	0	0
	25–34	721	674	28	25	0	0
	35–44	488	461	21	19	1	1
	45–54	367	355	19	18	2	0
	55+	339	277	34	28	0	0
	No data	2	1	0	0	0	0
II	15–24	982	873	27	25	0	2
	25–34	815	763	30	28	0	2
	35–44	545	517	26	24	0	0
	45–54	418	380	29	24	1	3
	55+	333	240	19	16	1	0
	No data	3	2	2	1	0	0
III	15–24	1314	1153	34	30	0	0
	25–34	780	729	30	26	1	3
	35–44	725	657	46	41	1	0
	45–54	464	386	28	27	0	2
	55+	529	414	38	32	0	0
	No data	0	0	2	2	0	0

Appendix Table XI Contd....

3. K A L A H A S T I

Survey	Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
						M+	C+
			M a l e s				
I	15–24	2106	1768	80	62	9	0
	25–34	2033	1706	165	147	24	6
	35–44	1530	1303	157	140	15	5
	45–54	957	817	133	127	13	8
	55+	973	659	148	130	12	13
	No data	14	8	2	2	0	0
II	15–24	2298	1872	89	81	7	9
	25–34	2401	2027	221	200	25	36
	35–44	1708	1460	234	218	17	26
	45–54	1002	838	177	159	11	17
	55+	815	663	162	145	2	12
	No data	101	48	33	23	0	0
III	15–24	2629	2236	77	68	7	5
	25–34	2675	2110	139	115	15	10
	35–44	1911	1748	211	185	22	24
	45–54	1253	1102	219	194	12	15
	55+	994	819	169	141	12	13
	No data	0	0	5	3	0	0
			F e m a l e s				
I	15–24	2130	1788	49	46	5	2
	25–34	2010	1740	84	76	9	2
	35–44	1339	1195	68	61	6	4
	45–54	1109	956	87	79	3	3
	55+	1013	663	76	64	2	2
	No data	15	8	19	15	0	1
II	15–24	2398	1882	71	59	4	4
	25–34	2352	1995	110	92	10	8
	35–44	1507	1296	100	88	6	14
	45–54	1277	1064	105	90	3	7
	55+	868	597	74	59	0	3
	No data	87	46	20	19	0	0
III	15–24	2814	2297	60	58	5	3
	25–34	2478	2166	87	76	4	2
	35–44	1728	1563	103	95	8	3
	45–54	1270	1078	86	75	3	1
	55+	1300	953	112	95	2	2
	No data	0	0	0	0	0	0

Contd.....

Appendix Table XI Contd....

4. R A J A M P E T

Survey	Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
						M+	C+
			M a l e s				
I	15-24	1023	897	52	46	5	1
	25-34	861	770	76	58	5	0
	35-44	715	659	105	77	8	1
	45-54	495	453	96	81	10	2
	55+	445	403	120	100	6	4
	No data	5	4	0	0	0	0
II	15-24	936	651	39	26	4	2
	25-34	944	749	65	56	7	4
	35-44	732	582	79	69	15	2
	45-54	443	367	65	61	4	2
	55+	396	301	75	64	8	3
	No data	3	2	0	0	0	0
III	15-24	945	748	42	36	4	4
	25-34	913	787	70	64	10	8
	35-44	844	709	80	68	9	12
	45-54	546	481	74	70	5	6
	55+	476	383	90	81	4	12
	No data	0	0	4	3	0	0
			F e m a l e s				
I	15-24	917	793	33	28	4	0
	25-34	925	852	54	43	5	0
	35-44	619	571	61	49	2	3
	45-54	507	470	62	58	2	3
	55+	463	386	81	68	4	0
	No data	8	6	0	0	0	0
II	15-24	933	638	18	14	1	1
	25-34	941	706	34	28	2	1
	35-44	621	479	28	24	1	1
	45-54	497	376	34	29	0	1
	55+	404	240	32	23	1	0
	No data	7	5	0	0	0	0
III	15-24	1184	844	19	15	1	2
	25-34	1051	792	32	26	0	0
	35-44	757	604	35	31	4	3
	45-54	490	389	41	38	3	1
	55+	605	370	37	31	0	4
	No data	0	0	3	2	0	0

Contd.....

Appendix Table XI Contd.....

5. C H I N T H A M A N I

Survey	Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases M+	Bacillary Cases C+
			M a l e s				
I	15-24	1551	1359	27	22	0	1
	25-34	1355	1211	63	55	6	1
	35-44	1023	928	66	56	3	0
	45-54	690	636	68	52	1	3
	55+	670	567	86	71	2	3
	No data	0	0	0	0	0	0
II	15-24	1691	1178	38	32	1	0
	25-34	1789	1241	57	53	2	4
	35-44	908	674	71	58	2	3
	45-54	718	534	59	53	3	3
	55+	625	417	67	60	1	2
	No data	5	2	1	1	0	0
III	15-24	1863	1533	30	29	3	4
	25-34	1649	1221	34	29	4	1
	35-44	1304	1110	49	45	4	4
	45-54	875	743	56	49	3	3
	55+	876	624	89	79	3	5
	No data	0	0	2	2	0	0
			F e m a l e s				
I	15-24	1685	1512	49	39	4	1
	25-34	1312	1239	74	68	9	5
	35-44	900	848	53	51	3	3
	45-54	669	620	64	52	0	1
	55+	545	423	58	49	2	0
	No data	0	0	0	0	0	0
II	15-24	1753	1248	49	43	0	2
	25-34	1528	1195	75	68	5	4
	35-44	957	754	51	45	2	0
	45-54	692	511	42	37	0	1
	55+	467	249	29	23	1	0
	No data	6	3	4	4	0	0
III	15-24	2152	1704	33	30	0	0
	25-34	1500	1330	55	49	2	3
	35-44	1155	947	52	49	0	4
	45-54	699	547	31	31	1	0
	55+	699	419	42	36	2	1
	No data	6	3	4	4	0	0

Contd.....

Appendix Table XI Contd.....

6. T I R U T T A N I

Survey	Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
						M+	C+
			M a l e s				
I	15–24	706	596	37	27	1	2
	25–34	729	624	44	35	4	1
	35–44	649	560	56	43	8	5
	45–54	396	356	55	45	3	2
	55+	376	333	74	65	5	0
	No data	5	1	0	0	0	0
II	15–24	820	694	26	23	3	0
	25–34	929	800	71	65	4	1
	35–44	723	635	78	73	4	2
	45–54	449	396	82	78	4	2
	55+	363	295	75	68	2	3
	No data	6	0	5	5	0	0
III	15–24	982	828	24	14	2	2
	25–34	1152	944	38	33	6	1
	35–44	781	711	63	52	8	3
	45–54	542	520	44	39	5	2
	55+	579	438	54	45	3	4
	No data	0	0	0	0	0	0
			F e m a l e s				
I	15–24	755	631	14	13	0	0
	25–34	879	800	37	33	2	0
	35–44	561	526	31	27	1	0
	45–54	463	407	34	31	1	0
	55+	315	240	31	26	1	0
	No data	5	3	0	0	0	0
II	15–24	925	746	29	23	0	1
	25–34	960	841	53	51	1	1
	35–44	624	542	37	34	0	0
	45–54	494	415	53	48	2	1
	55+	324	247	36	28	0	1
	No data	4	1	6	5	0	0
III	15–24	1114	987	15	11	1	3
	25–34	1107	987	26	21	1	3
	35–44	639	581	36	32	2	1
	45–54	620	500	35	29	3	0
	55+	519	385	29	21	0	0
	No data	0	0	0	0	0	0

Contd.....

Appendix Table XI Contd.....

Basic data obtained at Prevalence Survey III

1. R A Y A C H O T I

Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
					M+	C+
			M a l e s			
15–24	1419	1267	68	68	0	5
25–34	1220	1072	107	104	14	11
35–44	970	885	149	142	9	13
45–54	664	611	116	112	7	11
55+	643	564	170	167	4	15
No data	0	0	7	6	0	1
			F e m a l e s			
15–24	1293	1068	41	37	3	3
25–34	1247	1136	67	63	1	2
35–44	766	719	53	51	2	4
45–54	567	519	54	50	2	1
55+	728	624	93	90	3	1
No data	0	0	4	3	0	1

2. S R I N I V A S A P U R

Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
					M+	C+
			M a l e s			
15–24	697	568	11	10	0	0
25–34	552	463	8	8	0	3
35–44	447	374	27	24	1	3
45–54	297	251	17	14	2	1
55+	390	323	49	45	2	7
No data	1	0	1	1	0	0
			F e m a l e s			
15–24	688	568	14	12	0	0
25–34	586	514	19	17	0	1
35–44	348	308	15	14	0	1
45–54	339	297	28	25	1	0
55+	264	191	21	20	1	0
No data	1	0	1	1	0	0

3. M U L B A G A L

Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
					M+	C+
			M a l e s			
15–24	1179	979	22	21	0	1
25–34	1096	878	25	23	1	1
35–44	822	671	35	32	0	3
45–54	513	427	52	50	2	4
55+	560	467	66	59	3	6
No data	21	19	3	3	0	1
			F e m a l e s			
15–24	1106	851	15	14	2	2
25–34	1132	971	28	25	1	2
35–44	629	554	24	24	0	2
45–54	548	487	23	23	0	2
55+	506	373	44	39	0	0
No data	15	9	0	0	0	0

4. N A G A R I

Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
					M+	C+
			M a l e s			
15–24	570	491	17	16	1	1
25–34	565	504	32	29	7	2
35–44	565	504	42	42	3	9
45–54	335	295	45	42	5	5
55+	293	257	47	43	2	1
No data	0	0	0	0	0	0
			F e m a l e s			
15–24	699	595	10	10	0	0
25–34	663	611	17	14	1	0
35–44	432	394	20	20	3	1
45–54	347	327	29	26	0	0
55+	312	238	26	25	0	0
No data	2	2	0	0	0	0

Contd.....

Appendix Table XI Contd.....

5. P U T T U R

Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
					M+	C+
			M a l e s			
15–24	923	756	26	25	1	0
25–34	764	631	64	57	6	6
35–44	746	631	70	68	9	4
45–54	402	331	62	59	8	5
55+	354	302	50	46	5	3
No data	3	1	1	1	0	0
			F e m a l e s			
15–24	997	831	23	20	2	1
25–34	772	691	35	33	1	1
35–44	545	500	26	24	0	2
45–54	438	388	38	35	0	2
55+	351	257	33	31	1	1
No data	4	3	2	2	1	0

6. P U N G A N U R

Age Group	Eligible Population	X-Rayed	Selected for Bact.	Examined Bact.	Bacillary Cases	
					M+	C+
			M a l e s			
15–24	1527	1205	28	26	3	2
25–34	1272	1039	43	40	5	4
35–44	959	788	51	47	8	4
45–54	624	515	45	42	2	2
55+	661	545	88	83	2	5
No data	11	8	4	3	0	0
			F e m a l e s			
15–24	1671	1361	36	31	3	0
25–34	1164	1034	27	23	1	1
35–44	831	752	44	42	4	3
45–54	662	574	46	44	1	0
55+	692	477	53	49	1	2
No data	10	6	4	3	0	0

Appendix Table XII

"TREATMENT" TOWNS

Cases of bacillary pulmonary tuberculosis per 1000 by sex and age at Surveys I, II and III.

Towns	Age Groups	I		II		III	
		M	F	M	F	M	F
KADIRI							
	15–	8.6	3.4	4.8	2.8	3.6	4.4
	25–	11.6	6.2	9.5	6.9	10.8	11.0
	35–	29.5	8.6	13.3	5.4	26.6	4.3
	45–	30.8	6.7	15.1	2.3	21.5	2.6
	55+	15.4	7.6	15.5	9.2	34.7	3.5
	all	16.9	5.9	10.2	8.1	15.5	6.1
PALMANER							
	15–	0	0	1.5	2.5	5.1	0
	25–	7.5	0	8.1	2.8	4.5	6.3
	35–	14.0	4.8	5.3	0	8.3	1.7
	45–	11.0	6.0	10.7	12.7	9.3	5.4
	55+	12.8	0	3.7	5.0	17.9	0
	all	8.0	1.8	5.5	3.8	7.7	2.3
KALAHASTI							
	15–	6.6	4.2	9.4	5.1	6.1	3.6
	25–	19.7	7.0	33.3	10.8	14.3	3.2
	35–	17.2	9.3	31.6	17.5	30.0	7.6
	45–	26.9	6.9	37.2	11.0	27.7	4.3
	55+	43.2	7.2	23.6	6.3	36.6	4.9
	all	19.5	6.6	25.8	9.9	19.3	4.5
RAJAMPET							
	15–	7.6	5.9	13.8	4.0	12.5	4.5
	25–	8.5	7.4	17.1	5.2	25.0	0
	35–	18.6	10.0	33.4	4.9	34.9	13.1
	45–	31.4	11.4	17.4	3.1	24.2	11.1
	55+	29.8	12.3	42.8	5.8	46.4	12.9
	all	16.2	8.9	22.7	4.6	26.7	7.0
CHINTAMANI							
	15–	0.9	4.2	1.0	1.8	4.7	0
	25–	6.6	12.3	5.2	8.3	4.8	4.2
	35–	6.8	7.4	9.1	8.0	7.9	4.5
	45–	8.2	2.0	12.5	2.2	9.2	1.8
	55+	10.7	5.6	8.0	5.1	14.4	8.4
	all	5.1	6.7	5.8	4.2	7.3	3.0
TIRUTTANI							
	15–	6.9	0	4.9	1.7	8.3	5.5
	25–	10.1	2.8	6.8	2.5	8.5	5.0
	35–	30.2	2.2	10.1	0	18.7	5.8
	45–	17.2	2.7	15.9	8.0	15.2	7.2
	55+	17.1	5.0	18.7	5.2	19.2	0
	all	15.8	2.2	9.6	2.9	12.9	5.0

Contd.....

Appendix Table XII contd...

'CONTROL' TOWNS

Cases of bacillary pulmonary tuberculosis per 1000 by sex and age at Survey III.

Age Groups	M	F	M	F	M	F
	RAYACHOTI		SRINIVSAPUR		MULBAGAL	
15-	4.0	6.2	0	0	1.1	5.0
25-	24.0	2.8	6.5	2.2	2.5	3.5
35-	26.1	8.7	12.0	3.5	4.9	3.6
45-	30.5	6.2	14.5	3.8	14.6	4.1
55+	34.3	6.6	30.3	5.5	21.6	0
All	20.9	5.8	10.5	2.3	6.6	3.6
	NAGARI		PUTTUR		PUNGANUR	
15-	4.3	0	1.4	4.2	4.5	2.6
25-	19.7	2.0	21.4	3.1	9.3	2.3
35-	23.8	10.2	21.2	4.3	16.5	9.8
45-	36.3	0	41.3	5.6	8.3	1.8
55+	12.8	0	28.8	8.3	13.6	6.8
All	18.4	2.3	18.9	4.6	9.7	4.2

Appendix Table XIII

Distribution of bacillary cases at the three surveys according to Isoniazid Sensitivity*)

Towns	Positive by Microscopy						Positive by Culture only					
	Males			Females			Males			Females		
	S	R	N	S	R	N	S	R	N	S	R	N
'TREATMENT' Towns												
						Survey I (1960-61)						
Kadiri	34	7	6	12	2	2	19	1	0	5	0	1
Palmaner	9	0	3	1	1	1	2	0	0	1	0	0
Kalahasti	53	12	8	12	11	2	29	3	0	11	3	0
Rajampet	26	4	4	14	3	0	8	0	0	6	0	0
Chintamani	7	4	1	7	6	5	6	2	0	9	1	0
Tiruttani	16	2	3	3	2	0	8	2	0	0	0	0
						Survey II (1962-64)						
Kadiri	9	13	8	6	5	4	7	2	0	1	2	0
Palmaner	3	1	0	2	0	0	10	0	0	2	5	0
Kalahasti	42	20	0	8	14	1	78	20	2	29	6	1
Rajampet	20	16	2	3	2	0	10	3	0	2	2	0
Chintamani	3	5	1	0	8	0	6	5	1	3	4	0
Tiruttani	13	4	0	2	1	0	6	2	0	4	0	0
						Survey III(a) (1965-68)						
Kadiri	19	11	0	11	4	0	45	4	0	6	7	0
Palmaner	14	0	0	2	0	0	7	0	0	4	1	0
Kalahasti	45	22	1	17	5	0	52	15	0	9	2	0
Rajampet	17	15	0	4	3	1	33	9	0	8	2	0
Chintamani	10	6	1	3	2	0	13	4	0	7	1	0
Tiruttani	19	5	0	4	3	0	8	3	1	8	0	0
'CONTROL' Towns												
						Survey III(b) (1965-68)						
Rayachoti	14	8	2	5	5	1	52	3	1	9	2	1
Srinivasapur	2	3	0	1	1	0	11	3	0	2	0	0
Mulbagal	4	2	0	0	1	2	13	3	0	5	3	0
Nagari	9	9	0	4	0	0	17	1	0	1	0	0
Puttur	25	4	0	4	0	1	17	1	0	6	1	0
Punganur	16	4	0	8	2	0	15	0	1	5	2	0

*) Note: S = Isoniazid sensitive strains.
R = Isoniazid resistant strains.
N = Sensitivity tests not available.

Appendix Table XIV

Comparison of Prevalences at Surveys I, II & III in the INH-PAS Towns vs. INH Towns - Rates = Cases per 1000 adult males & females

Sex	INH-PAS						INH ONLY					
	I		II		III		I		II		III	
A. Cases irrespective of bacillary INH sensitivity												
(i) Cases positive by Microscopy		%		%		%		%		%		%
Males	4.42	100	3.22	59**	3.48*	64*	4.45	100	4.32	97	3.85	87
Females	1.64	100	1.50	91**	1.14	70*	2.18	100	1.00	46	1.11	51
Both Sexes	7.06	100	4.72	67**	4.62	65	6.63	100	5.32	80	4.97	75
(ii) Cases positive by Culture only												
Males	2.03	100	3.69	182	3.63	179	1.73	100	2.07	120	3.79	219
Females	0.72	100	1.62	225	0.99	138	0.74	100	0.92	124	1.43	193
Both Sexes	2.75	100	5.31	193	4.62	168[1]	2.46	100	2.99	122	5.22	212
(iii) All positive cases												
Males	7.45	100	6.92	93	7.11	95	6.18	100	6.39	103	7.64	124
Females	2.36	100	3.13	133	2.12	90	2.93	100	1.92	66	2.54	87
Both Sexes	9.80	100	10.05	103	9.23	94	9.11	100	8.31	91	10.18	112
B. Cases with INH-Sensitive strains												
(i) Cases positive by Microscopy												
Males	4.65	100	1.84	40	2.58	55	3.77	100	2.55	68	2.47	66
Females	1.08	100	0.78	72	0.88	81	1.51	100	0.39	26	0.64	42
Both Sexes	5.73	100	2.62	46	3.46	60	5.28	100	2.94	56	3.11	59
(ii) Cases positive by Culture only												
Males	1.90	100	3.05	161	3.14	165	1.46	100	1.45	99	2.92	200
Females	0.64	100	1.03	161	0.64	100	0.70	100	0.58	83	1.25	179
Both Sexes	2.54	100	4.08	161	3.78	149	2.16	100	2.03	94	4.17	193
(iii) All positive cases												
Males	6.55	100	4.89	75	5.72	87	5.23	100	4.00	76	5.39	103
Females	1.72	100	1.81	105	1.52	88	2.21	100	0.97	44	1.89	86
Both Sexes	8.27	100	6.70	81	7.24	88	7.45	100	4.97	67	7.28	98
C. Cases with INH-Resistant Strains												
(i) Cases positive by Microscopy												
Males	0.76	100	1.38	182	0.90	118	0.67	100	1.77	264	1.38	206
Females	0.55	100	0.73	133	0.25	45	0.67	100	0.61	91	0.47	70
Both Sexes	1.31	100	2.11	161	1.16	89	1.34	100	2.38	178	1.85	138
(ii) Cases positive by Culture only												
Males	0.14	100	0.63	450	0.49	350	0.26	100	0.61	235	0.87	335
Females	0.08	100	0.60	750	0.35	438	0.04	100	0.34	850	0.18	450
Both Sexes	0.22	100	1.22	555	0.84	382	0.30	100	0.95	317	1.05	350
(iii) All positive cases												
Males	0.90	100	2.01	223	1.39	154	0.93	100	2.39	257	2.25	242
Females	0.63	100	1.32	210	0.60	95	0.71	100	0.94	132	0.65	92
Both Sexes	1.53	100	3.33	218	1.99	130	1.64	100	3.33	203	2.90	177

1) P = 0.06

Appendix Table XV

Comparison of the prevalence in the 6 'Treatment' Towns and the 6 'Control' Towns at the Sample Survey 1959 and at Survey III, 1965-68 - both sexes, cases per 1000 adults.

Towns	Sample Survey 1959 (S1)		Survey III 1965-68 (S3)		$S_1 - S_3$	
	Prevalence	Variance	Prevalence	Variance	Mean Changes	Variance
(i) Cases positive by Microscopy						
'Treatment' Towns						
Kadiri	4.33	0.55	4.60	0.01	-0.27	0.56
Palmaner	3.21	0.54	2.87	0.03	0.38	0.57
Kalahasti	9.98	0.45	6.35	0.08	3.63	0.53
Rajampet	10.26	1.59	6.94	0.18	3.32	1.77
Chintamani	3.22	0.40	2.48	0.06	0.74	0.46
Tiruttani	4.54	0.62	5.44	0.27	-0.90	0.90
			Weighted Mean Change : 1.118			
'Control' Towns						
Nagari	5.61	0.55	5.53	0.08	0.08	0.63
Srinivasapur	6.02	1.03	0.08	0.12	3.94	1.15
Mulbagal	1.81	0.28	1.48	0.01	0.33	0.29
Punganur	1.81	0.16	3.92	0.08	-2.11	0.24
Puttur	7.88	0.70	6.73	0.08	1.15	0.77
Rayachoti	11.19	2.25	5.53	0.02	5.65	2.27
			Weighted Mean Changes: 1.375			
			Difference = -0.257			
			Variance of Difference: 9.454			
			t_{10} = -0.084, P: >0.2			
(ii) Cases positive by Culture only						
'Treatment' Towns						
Kadiri	5.14	0.61	6.31	0.06	-1.17	0.67
Palmaner	2.22	0.44	2.06	0.03	0.16	0.46
Kalahasti	7.62	0.28	5.44	0.09	-2.12	0.37
Rajampet	3.41	0.37	9.42	0.46	-6.01	0.82
Chintamani	1.29	0.16	2.72	0.04	-1.43	0.20
Tiruttani	3.41	0.44	3.51	0.07	-0.10	0.51
			Weighted Mean Change : 1.049			
'Control' Towns						
Nagari	3.38	0.32	4.65	0.06	-1.26	0.38
Srinivasapur	1.23	0.24	4.50	0.12	-3.27	0.36
Mulbagal	1.88	0.34	3.66	0.03	-1.78	0.36
Punganur	2.67	0.20	3.00	0.05	-0.34	0.26
Puttur	4.46	0.40	5.10	0.13	-0.63	0.53
Rayachoti	1.02	0.14	8.03	0.03	-7.01	0.17
			Weighted Mean Change : -2.394			
			Difference = 1.345			
			Variance of difference: 2.148			
			t_{10} = 0.918; P: >0.2			

Contd.....

Towns	Sample Survey 1959 (S1)		Survey III 1965-68 (S3)		S1 - S3	
	Preva-lence	Vari-ance	Preva-lence	Vari-ance	Mean Changes	Vari-ance
(iii) All positive cases						
'Treatment' Towns						
Kadiri	9.47	1.32	10.91	0.07	-1.44	1.39
Palmaner	5.43	1.07	4.93	0.16	0.50	1.23
Kalahasti	17.60	1.02	11.85	0.19	5.75	1.21
Rajampet	13.67	2.35	16.36	0.71	-2.69	3.06
Chintamani	4.51	0.60	5.20	0.14	-0.69	0.74
Tiruttani	7.95	1.29	8.94	0.25	-1.00	1.54
			Weighted Mean Changes:		0.144	
'Control' Towns						
Nagari	9.00	1.02	10.18	0.18	-1.18	1.20
Srinivasapur	7.26	1.36	6.58	0.30	0.68	1.66
Mulbagal	3.68	0.63	5.14	0.02	-1.46	0.65
Punganur	4.48	0.44	6.92	0.13	-2.44	0.57
Puttur	12.34	1.32	11.83	0.25	0.52	1.57
Rayachoti	12.20	2.53	13.56	0.08	-1.36	2.60
			Weighted Mean Changes:		-0.909	
			Difference =		1.058	
			Variance of difference:		1.418	
			t_{10} =		0.884; P: > 0.2	

Appendix Table XVI

Comparison of Mean Prevalences of the 12 Towns at the Sample Survey 1959 and Survey III 1965-68 - Cases per 1000.

		Survey 1959 (S1)	Survey 1965-68 (S3)	Mean change @) (S1-S3)	Variance of mean change	t (11d.f)	P
Males							
	M+	8.89	6.94	1.78**	1.57	1.42	0.2
	C+	4.13	7,58	-3.47	1.39	-2.95	0.01
	all	13.02	14.52	-1.62	1.46	-1.34	0.2
Females							
	M+	2.63	2.06	0.50	0.44	0.75	> 0.2
	C+	2.16	2.15	-0.03	0.40	-0.04	> 0.2
	all	4.79	4.21	0.51	1.27	0.45	> 0.2
Both Sexes							
	M+	5.82	4.50	1.24*	0.40	1.97	0.07
	C+	3.14	4.87	-1.73	0.56	-2.31	0.04
	all	8.97	9.37	-0.39	0.42	-0.60	> 0.2

Note: @) Weighted Mean Change

M+ denotes cases positive by microscopy.
C+ denotes cases positive by culture only.